Transcriptional and physiological analysis of the model cyanobacterium *Synechocystis* PCC 6803 under ethanologenic and external ethanol conditions

DISSERTATION

zur Erlangung des akademischen Grades

d o c t o r r e r u m n a t u r a l i u m

(Dr.rer.nat.)

in Fach Biologie

eingereicht an der

Mathematisch-Naturwissenschaftlichen Fakultät I

der Humbold-Universität zu Berlin

von

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Datum der mündliche Prüfung: 30.01.2013

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Summary

Until recently, little has been known about the effects of ethanol on the physiology of cyanobacteria. This is not surprising as it is unlikely that cyanobacteria encounter growth inhibiting concentrations of ethanol in their natural environment, and thus the ethanol stress response used to be of limited interest to the scientific community. Nevertheless, for recent biotechnological approaches in the field of biofuel production, and in particular for the attempts to produce ethanol with the help of genetically modified microalgae and cyanobacteria, knowledge of cellular tolerance and response to the desired product is pivotal. In the course of this work, first examinations of an ethanologenic mutant of *Synechocystis sp*. PCC6803 revealed a severe "bleaching" phenotype. Microarray analysis further corroborated this physiological effect by demonstrating that a specific part of the phycocyanin operon is the most significantly and strongly affected functional genetic subsystem under ethanol producing conditions. Northern blot studies of the phycocyanin operon (*cpcBAC2C1D*) revealed a specific, short novel transcript that was attributed to *cpcA*. Photometrical measurements of the phycocyanin absorption further confirmed this result. Additional microarray experiments with different concentrations of external ethanol and different time points showed a time-delayed response (24h) characterized by a prominent up-regulation of PS II genes with phycocyanin linker proteins playing a major role in the transcriptional response. A Strong overlap in the response of ethanol treated and ethanol producing *Synechocystis sp*. PCC6803 cultures was observed. Combined analyses of the microarray experiments indicated thioredoxin modulated processes as a major part in the cellular response. Another aspect of this work was an artificial evolution experiment, which was performed to delineate the intrinsic capacity of *Synechocystis sp*. PCC6803 to tolerate ethanol. This was done by long-term cultivation of *Synechocystis sp*. PCC6803 in ethanol containing medium and resulted in a variant that showed a higher tolerance to ethanol than the ancestral strain as judged by direct comparison of growth characteristics. In addition, the evolved strain proved to be a superior background for endogenous ethanol production showing that artificial evolution experiments are a suitable method to improve certain features of organisms for biotechnological purposes. Overall, the results of this work give new insight into physiological and gene regulatory responses of *Synechocystis sp*. PCC6803 exposed to ethanol and will be a very valuable dataset for future attempts to improve cyanobacterial ethanol production by the means of genetic engineering.

Zusammenfassung

Bis zum heutigen Zeitpunkt ist wenig über die physiologischen Effekte von Ethanol auf Cyanobakterien bekannt. Dies ist nicht überraschend, da es unwahrscheinlich ist, dass Cyanobakterien in ihrer natürlichen Umwelt auf Wachstums inhibierende Konzentrationen stoßen, und deswegen war die Stressantwort auf Ethanol nur von geringerem Interesse für die Forschungsgemeinschaft. Nichts desto weniger sind durch neue Entwicklungen im Biofuel-Sektor, insbesondere im Kontext der Produktion von Ethanol mit Hilfe von genetisch manipulierten Cyanobakterien, Kenntnisse über die zelluläre Toleranz und Zellantwort gegenüber dem gewünschten Produkt von grundlegender Bedeutung. Erste Experimente mit ethanologenen *Synechocystis sp*. PCC6803, die im Laufe dieser Arbeit gemacht wurden, zeigten einen „bleaching“ Phänotyp. Microarray-Experimente, die einen Einblick in die zelluläre Antwort durch Änderung der Genexpression auf Ethanolproduktion bringen sollten, zeigten, dass Gene des Phycocyanin-Operons als die am signifikantesten und stärksten betroffenen funktionalen genetischen Elemente. RNA blot-Analysen der Gene *cpcBAC2C1D* des Phycocyanin-Operons identifizierten ein Ethanol spezifisches Signal das dem *cpcA* signal zugeschrieben werden kann. Photometrische Messungen der Absorption des Lichts durch Phycocyanin konnten des Weiteren diese Ergebnisse auf der metabolischen Ebene bestätigen. Weitere Microarray-Experimente mit verschiedenen Konzentrationen von extern zugefügtem Ethanol und zu verschiedenen Zeitpunkten zeigten eine zeitverzögerte Antwort (24h), charakterisiert durch eine prominente Hochregulation von PS II-Genen und dem Transkript cpcG2. Es zeigte sich eine hohe Übereinstimmung der Zellantwort von Ethanol-produzierenden und mit Ethanol behandelten Zellen. Weitere Ergebnisse der Microarray-Experimente deuteten auf durch Thioredoxin beeinflusste Prozesse als wichtigen Bestandteil der zellulären Antwort auf Ethanol hin. Diese Arbeit beschreibt weiterhin die Ergebnisse eines Experiments zur "Evolution im Labor", das die intrinsische Kapazität von *Synechocystis sp*. PCC 6803 zur Erweiterung der Toleranz gegenüber Ethanol aufzeigen sollte. Dies wurde durch Langzeit-Kultivierung von *Synechocystis sp*. PCC6803 in Ethanol-haltigem Medium erzielt. Wie Wachstumsvergleiche mit dem Ausgangsstamm zeigten, resultierte dies in einer Varianten mit erhöhter Ethanoltoleranz. Die erhöhte Ethanoltoleranz führte zu einer Optimierung der endogenen Ethanolproduktion. Derartige Versuche zur Stammoptimierung durch "Evolution im Labor" sollten daher geeignete Mittel sein, um bestimmte Eigenschaften von Organismen für biotechnologische Ziele zu verbessern. In der Gesamtheit geben die Ergebnisse dieser Arbeit Einblicke in die Antwort der *Synechocystis*-Zellen auf Ethanol auf den Ebenen des Stoffwechsels und der Genexpression und stellen eine wertvolle Datensammlung für zukünftige Versuche mit dem Ziel dar, die Ethanolproduktionsrate in Cyanobakterien durch genetic engineering zu erhöhen.

1 Introduction

1.1 Current biofuel production technologies: first-, second-, and third-generation processes

Plants and cyanobacteria are photoautotrophs and thus belong to the category of most important primary producers in our biosphere. They use the energy of sunlight and water as an electron donor to fix carbon and release oxygen through a process known as photosynthesis. Thus, plants and algae form the basis for virtually the entire world's food and fuel consumption, and together with cyanobacteria, which form a group of photosynthetic bacteria, supply our atmosphere with oxygen (Medigan *et al.* 2000). The plant material-based production of ethanol is a classical example for a "first generation" biofuel generation process. Plants store most of the energy derived from oxygenic photosynthesis in the form of sugars and polysaccharides. They can be found as intracellular sucrose and starch, or as polymers in the cell wall, e.g. cellulose, hemicellulose and lignin. Most suitable for biofuel production are sucrose and starch, as they can be directly fermented to alcohols like ethanol, propanol or butanol (Woods, 1995). Using other plant components requires more cost intensive up-stream processing, e.g. heat and acid treatment (Van Wijk, 2001; Mosier *et al.*, 2005). After such treatments the rest of the biomass can be used for further biofuel synthesis processes, e.g. methane fermentation and also for the food industry (Marris, 2006; Buerkert and Schlecht, 2009). Second generation biofuel production is based on the observation that certain species produce high amounts of lipids as triglycerides or poly-isoprenoids when they were deprived of nitrogen (Metzger and Largeau, 2005; Ratledge 2004). These lipids can be used as biodiesel after transesterification with methanol. In literature, another process can be found termed 'second generation biofuel processes', namely the conversion of material like lignocellulose into ethanol. Third generation biofuel production - which is also the starting point of this work - is based on genetic modification to make an organism produce a desired biofuel directly, without the need of harvesting or further treatment. An example of a third generation biofuel which is produced by cyanobacteria was first described by Deng and Coleman (Deng and Coleman, 1999), who introduced a fermentative pathway for ethanol production from the alpha-proteobacterium *Zymomonas mobilis (Z.mobilis)* into a cyanobacterium in order to create a biofuel producing "cellular factory".

1.2 Cyanobacterial diversity

Cyanobacteria (also called "blue-green algae") belong to the oldest organisms on earth. Fossil records date nearly as far as 3.5 billion years back (Schopf, 1993). 1.5 billion years back, these organisms played a pivotal role in the creation of our vital atmosphere by the enrichment of the planetary oxygen (Des Marais *et al.*, 1991). Cyanobacteria are photoautotrophs performing oxygenic photosynthesis by taking advantage of chlorophyll (Chl) *a* associated with photosystems (PS) I and II. The term cyanobacteria derives from the greek word κυανός (kyanós), which means blue and comes from the phycobilin pigment phycocyanin (PC) which gives this phylum of the domain bacteria its characteristic blue-ish color. Cyanobacteria form a very heterogeneous group of prokaryotes. They comprise unicellular, colonial and multicellular filamentous forms (Fig.1) (Stanier and Cohen-Bazire, 1977). Certain species also have the ability to differentiate into functional cell types like heterocysts for nitrogen (N) fixation, or akinetes as specialized type of resting cells. We are profiting from cyanobacteria on an extensive scale, starting from N fixation and thereby contributing to global soil and water fertility (Montoya *et al.*, 2004) to being one of the most important primary producers, as phytoplankton (which includes cyanobacteria) accounts for nearly 50 % of the net primary productivity of the biosphere (Field *et al.*, 1998).

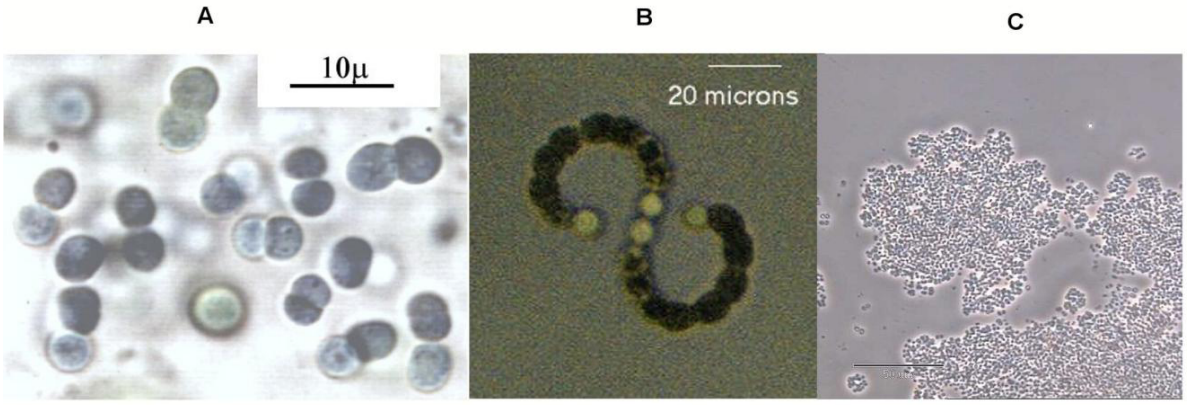

Figure 1: Exert of the variety of cyanobacteria species. (A) Unicellular model organism *Synechocystis* sp. (B) Filamentous Anabaenopsis circularis with clearly visible central pair of heterocysts (C) Colony forming *Gloeobacter sp.* harboring a unique membrane composition (E. Selstam and Douglas Campbell, 1996).

(Images from *http://www.cyanosite.bio.purdue.edu/images/images.htm*)

The habitats of cyanobacteria are highly diverse. They can be found in fresh water as well as in seawater, on wet soil or even in deserts or hot springs. Some species live as symbionts in lichens or even in roots. One aspect of the scientific interest in cyanobacteria is based on the fact that they can cause considerable damage to human health and the environment. Under certain conditions cyanobacteria grow to very high densities, referred to as "blooms" which can negatively interact with i.e. the life stock. Various types of cyanobacteria, such

as *Microcystis*, *Anabaena and Planktothrix*, frequently form toxic blooms in freshwater lakes (Mur *et al.*, 1999). These blooms can be harmful to different ecosystems. Times of frequent eutrophications of waters as well as times of a rising global average temperature favor the overgrowth of algae in the waters which also leads to a diminishing of the original biodiversity (Paerl and Huisman, 2008).

1.3 Photosynthesis and Cyanobacteria

In plants photosynthesis is located in specialized organelles called chloroplasts. Chloroplasts have a number of morphological, biochemical and genetic properties, which are very similar to those of cyanobacteria. The stable uptake of cyanobacteria into a eukaryotic, non-photosynthetic host cell is believed to be the origin of the chloroplast organelle. This process of primary endosymbiosis was most likely a single event in the course of evolution (Douglas, 1998; Ezpeleta *et al.*, 2005). Sequencing of chloroplast genomes showed that the structure as well as the coding capacity of the plastid DNA is very similar to algae (Gray, 1993; Martin *et al.*, 2002). These both genetic characteristics are the strongest evidence for the monophyletic ancestry of chloroplasts. Very interestingly, only few differences can be found between the photosynthesis of plants and cyanobacteria. Though evolutionary very distant, the photosynthetic mechanisms of pro- and eukaryotes are remarkably similar (De Las Rivas *et al.*, 2004; Xu *et al.*, 2001). The light reaction of photosynthesis in chloroplasts and nearly all cyanobacteria - with the exception of *Gloeobacter violaceus* PCC 7421 (Rippka *et al.*, 1974) - is taking place in the thylakoid membrane. Therefore, the cyanobacterium *Synechocystis* sp. PCC6803 (hereafter *Synechocystis*) has become an important cyanobacterial model organism for studying basic photosynthetic processes in the last 20 years. *Synechocystis* is a mesophilic cyanobacterium, which was isolated from a fresh water lake in California (USA) (Stanier *et al.*, 1971). As early as 1982, genetic manipulation of this organism was achieved (Grigorieva & Shestakov, 1982). *Synechocystis* has a natural competence for DNA uptake and further harbors an effective recombination system to integrate foreign DNA into its genome. Another advantage of *Synechocystis* as a model organism for photosynthesis is its ability to grow heterotrophically (Rippka *et al.*, 1979; Williams, 1988), which permits the genetic knock out of essential components of the photosynthetic apparatus. In addition, it was the first photosynthetic organism whose genome was completely sequenced (Kaneko *et al.*, 1996). The genome of *Synechocystis* comprises 3, 6 x 10^6 basepairs (bp), coding for approximately 3300 proteins, only about half of which have a known function. The photosynthetic electron transport chain in cyanobacteria differs very little from that of the chloroplasts. The electrons can be transported in a cyclic and in a non-cyclic way. In both cases the produced proton gradient is used to generate ATP (Arnon *et al.*, 1959), while the reduction of $NADP^+$ is only possible by linear electron transport. In the Calvin-Cycle, whose function is to fix CO_2 into energy rich carbohydrates, ATP and $NADPH^+/H^+$ are used to reduce CO_2. These energy rich components are the fundament for photoautotrophic growth. Also the composition of PS I, PS II the Cytb6f complexes and the ATP-synthases of chloroplasts and cyanobacteria are very similar. These complexes differ mainly in the presence and absence of smaller non-essential components. Other differences can be found in PS I, which in contrast to plants, is

not always in a monomeric but rather in a trimeric form (Kouril *et al.*, 2005). Also the composition of the antenna system for photosynthesis is different. Cyanobacteria have membrane associated phycobilisomes. These protein complexes contain linear tetrapyrroles (phycobilin) as chromophore groups. Phycobilisomes are located on the cytoplasmic site of the thylakoid membranes and are associated with PS II, PS I, or both, depending on the light intensity and quality. The redistribution of the light harvesting complex is called state transition. Depending on the cyanobacterial species, the phycobilisomes consist of chromophores carrying the subunits allophycocyanin, phycoerythrin, PC, phycourobilin and/or phycoerythocyanin, as well as of structuring anchor and linker proteins. Depending on the constitution of the chromophore- carrying subunits, the phycobilisomes are enhancing the quantum yield by absorbing light at wavelengths between approximately 500 to 650 nm. The schematic structure of a phycobilisome antenna is shown in Fig.2.

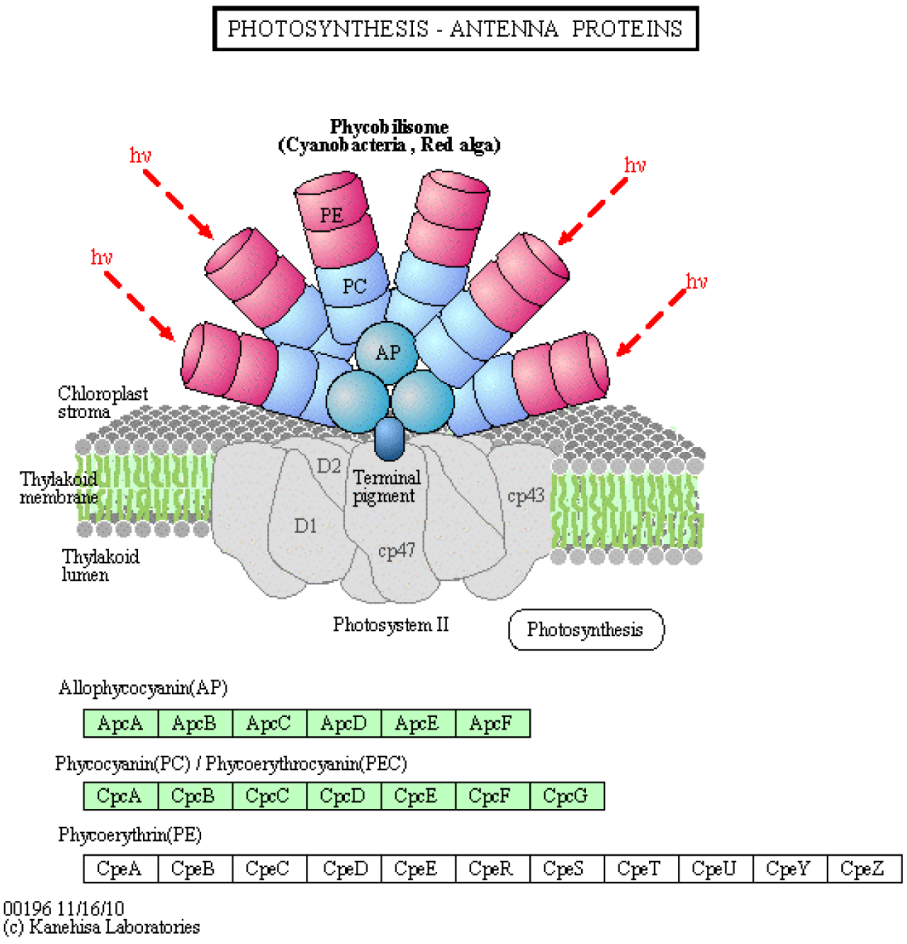

Figure 2: Model of cyanobacterial antenna proteins (from KEGG Database Pathways). Green color of visualized proteins indicates its presents in *Synechocystis*.

1.4 Regulatory systems in *Synechocystis*

Cyanobacteria are exposed to a variety of environmental signals, which have to be sensed to adequately adapt to the environment and to ensure survival. The connection between signal and cell response is often achieved by the so-called "regulatory two component systems" (Montgomery, 2007), serine/threonine-kinases (Zhang *et al.*, 2007) and second messengers. Two-component systems consists of proteins containing a signal transduction chain, typically one sensor kinase, and one response regulator (Chang and Stewart, 1998; Mizuna *et al.*, 1996). The sensor kinase senses changes in the environment over a sensor domain and passes the signal to a response regulator. The latter is responsible for changes in the expression of certain genes or influencing other cell processes according to the environmental signal. The majority of described output domains have DNA binding properties and are therefore often assigned as transcription factors (Parkinson and Kofoid, 1992). The transition of the information between sensor kinase and response regulator is achieved by phosphorylation (Li *et al.*, 2000). Most of the signal-transducing proteins contain one of the general signal domains for phosphor transfer, either a transmitter or a receiver domain (Mizuno *et al.*, 1996). A typical sensor kinase is carrying a sensor domain, as well as a transmitter domain. Furthermore, hybrid-histidine-kinases exist, harboring a kinase domain and a response regulator domain (Mizuno *et al.*, 1996). In certain cases, a histidine kinase can transfer the signal to multiple response regulators or vice versa (Laub, 2007). Through sequencing of the *Synechocystis* genome and comparative studies on organisms, 80 possible ORFs have been identified, among which 26 code for possible sensor kinases with a transmitter domain, 38 for possible response regulator as well as 16 for hybrid sensor kinases with both a transmitter and a receiver domain (Mizuno *et al.*, 1996). Today there are 47 histidine kinases and 45 response regulators known, which constitute about 2.5% of the genome (Ngarajan *et al.*, 2012). Gene expression is regulated at different levels: regulation at the transcription, post-transcriptional regulation, regulation of the translation and post-translational regulation. For transcription of eubacterial DNA, the RNA polymerase holoenzyme is composed of a sigma (σ) -subunit and a core enzyme (Ishihama *et al.*, 1993). RNA polymerization is the function of the core enzyme which requires the σ- subunit for specific binding to the promoter. Global transcriptional changes in *Synechocystis* are mainly resulting from the modulation of RNA polymerase promoter selectivity. This is achieved by altering the intracellular composition of σ-factors in response to environmental or cellular changes (Imamura and Asayama, 2009). Recent studies showed evolution based approaches to identify and subsequent manipulate such global regulators as an outperforming method to traditional approaches to quickly and more effectively optimizing phenotypes with desired properties for biofuel production (Alper *et al.*, 2007).

1.5 Aim of this work

The heterologous expression of the Z.moblis enymes pyruvate decarboxylase (PDC) and alcohol dehydrogenase (ADH) and subsequent ethanol production in the cynaobacterium Synechococcus sp. was described for the first time in 1999 (Deng and Coleman, 1999). At the time of this study, the synthetic system appeared still not stable and productive enough to be used in a commercial production units. This is not surprising, as the basic strategy for ethanol production in cyanobacteria is contradicting fundamental biological principles. First, ethanol production does not constitute an advantage for cyanobacteria. Therefore a single cell within a population that has a mutation stopping the ethanol production will have a selective advantage and overgrow the remaining cells. Second, ethanol production is detrimental to cyanobacteria. It is extremely unlikely that cyanobacteria ever in evolution experienced ethanol concentrations in the order of magnitude that would be commercially viable. Hence, it is unlikely that cyanobacteria developed ethanol-specific resistance mechanisms and the counter-selective pressure against the expression cassette further increases. Therefore understanding the cellular response of *Synechocystis* and knowing potential targets of ethanol is pivotal for approaches to minimize the negative effects of ethanol on *Synechocystis*. For cyanobacterial ethanol production it is also necessary to address some basic questions, for example to which extend photosynthesis and ethanol production are compatible processes and if "bottlenecks" that might make the production of ethanol by algae inefficient can be identified. With the help of transcription studies via Northern blotting and microarray experiments, combined with knockout studies of regulatory genes and physiological analyses, the stress ethanol and ethanol production is posing should be identified and characterized. Further questions which should be addressed are, if there are methods to increase ethanol tolerance and production rates in *Synechocystis* and if there is a connection between those two. Further questions which should be elaborated are, if a specific signal to ethanol can be identified and if cross-stress and adaptation experiments can yield information on the resistance mechanisms of *Synechocystis*.

2 Results and Discussion

2.1 Ethanol production

2.1.1 General properties ethanologenic *Synechocystis* in optimized photo bioreactors

In order to analyze the effects of ethanol production in *Synechocystis* under state of the art production conditions, a hybrid ethanologenic *Synechocystis* strain was provided by Cyano Biofuels GmbH. The strain harbors a production cassette containing the pyruvate decarboxylase of *Z. mobilis* and the probable alcohol dehydrogenase *adhA* from *Synechocystis* induced by copper depletion (see Material and methods chapter 3.2.16.).

A gradual difference in the visual color of the cultures between ethanologenic *Synechocystis* and the non-ethanologenic control strain could be observed. A more yellowish pigmentation of the ethanol producer compared to the rather blue-green reference strain was observed. This change in cellular pigment composition could be due to the change in quantity of Chl *a* and other pigments or pigment-containing complexes of *Synechocystis* such as PC or Car.

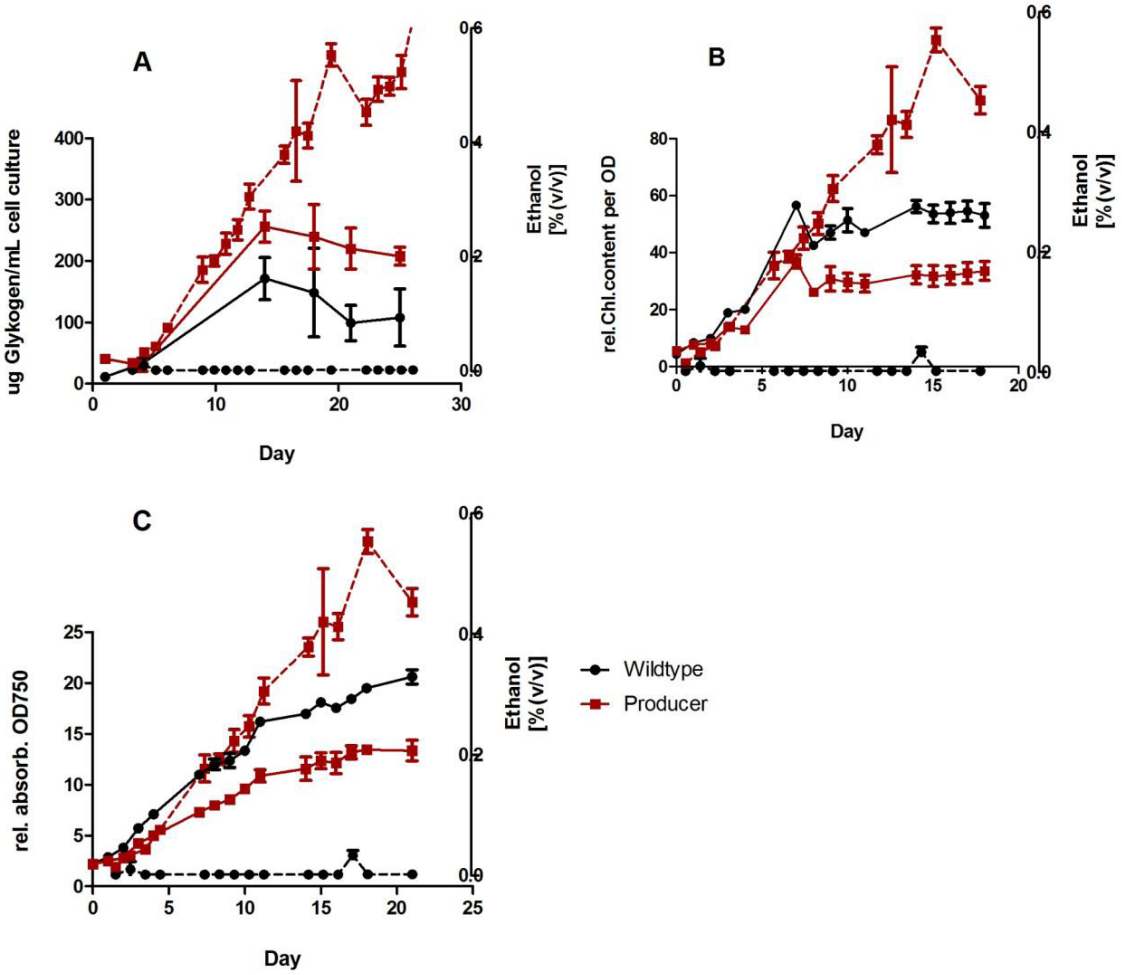

Figure 3: Effect of engineered ethanol production on growth, Chl *a* content and glycogen accumulation of *Synechocystis*. (A), (B) and (C) depict successive ethanol accumulation marked as dashed lines, representing the percentages of ethanol in the media in comparison to glycogen accumulation (A), normalized Chl *a* content (B) and optical density at 750 nm (OD_{750}) (C) represented in solid lines recorded up to 25 days after the induction. Circles and squares mark samples taken from the control strain and producer cultures, respectively. Each data point represents the mean of biological triplicates. The error bars denote standard deviations.

Monitoring the ethanol production over a period of 25 days revealed that the *Synechocystis* cells equipped with an introduced fermentation pathway and grown under specialized production environment are stably producing ethanol to a final concentration of 0.5 % (v/v) (Fig.3). Along with the production of ethanol, a significant higher accumulation of glycogen occurred in ethanol producing cultures compared to non-producing cultures (Fig.3A). The glycogen concentration was highest at the stationary phase (two weeks after the onset of the experiment) and then gradually declined in the time course. Glycogen is shown to play a role in the adaptation mechanisms of Saccharomyces italicus to ethanol (Patil *et al.*, 2011) and therefore the observed glycogen accumulation in ethanologenic *Synechocystis* could be a

result of an adaptation or a protective mechanism. While in the beginning of the experiment (day one to six both strains exhibited a similar Chl *a* content later on the ethanologenic *Synechocystis* cultures showed a drop in Chl *a* content in comparison to the control strain. With the progression of the experiment, which was accompanied by a rise of ethanol concentrations within the media and increase in the cell density of the cultures, the difference in relative Chl *a* content per OD_{750} dramatically increased between the ethanologenic and the control strain (Fig.3B), and thus most likely resulting in the reduced ability of the producer to utilize the incoming light.

2.1.2 Transcript accumulation of ethanologenic *Synechocystis* cultures

Microarray experiments, which have been performed in cooperation between Cyano Biofuels GmbH and the group of Prof. Dr. Wolfgang Hess (Experimental Bioinformatics, Albert-Ludwigs University of Freiburg; microarray hybridization and analysis (Dr. Jens Georg), revealed that even though dramatic loss of cell viability could be detected in the ethanologenic *Synechocystis* cultures during the course of the ethanol production, relatively few changes in the transcript accumulation could be observed. Certain genes which appeared to be relatively strong regulated in the conducted microarray experiments were selected for further verifications by Northern blot analysis (Fig.4). Only two of the mRNAs, namely *cpcB* and *rps8*, showed a strong and significant appearance (meaning that all different probes per annotated gene reacted in the same way under all tested time points; data not shown) in the microarray data. Nevertheless, the Northern blot analysis confirmed for all the selected candidates the differential mRNA accumulation in the producer to the control strain which were selected from the microarray data.

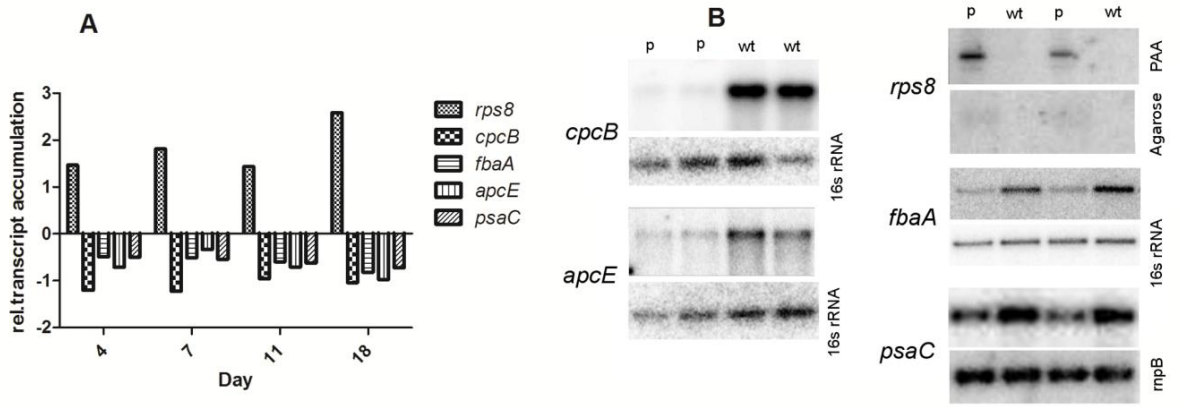

Figure 4: Transcript accumulation of selected mRNAs, detected by microarray experiments and verified by Northern blot analyses. Northern blot analyses (B) with probes for *cpcB, rps8, fbaA, apcE* and *psaC* with total RNA taken after 14 day of ethanol production and 1 μg used for each lane before the blotting on a nylon membrane and semi-quantitative analysis of the microarray data (A).

2.1.3 Microarray verification by Northern blot analyses

Microarray probes for *cpcB* showed a dramatic and very significant decrease of the corresponding mRNA under ethanologenic conditions in *Synechocystis* (Fig.4A). Northern blot analyses with a *cpcB*-specific probe confirmed that the functional bi-cistronic transcript of *cpcBA* (~1500 nt in length) vanished almost completely during ethanol production (Fig.4B). While the differential expressions of the other analyzed transcripts were not as striking as the one observed for *cpcB* and *rps8*, they certainly have to be taken into account. Microarray data analysis and Northern blot verification revealed three further specific changes in the mRNA accumulation under ethanologenic conditions. The changes include namely a down-regulation of apcE (slr0335), which is the corresponding transcript of a phycobilisome core-membrane linker polypeptide, than the down-regulation of the transcripts of the PS I subunit PsaC (ssl0563), and the down-regulation of the transcripts of an important glycolytic enzyme *FbaA* (sll0018). As in the case of transcripts of PC, the steady-state accumulation of these transcripts can also be traced back to toxicity of ethanol and for the case of *FbaA* and *Rps8* it will be shown later in this work (chapter 2.3.8.).

2.2 Global transcriptional analyzes of the ethanol treated and ethanologenic *Synechocystis*

2.2.1 Overall expression pattern and verification by Northern blot analyses

Table 1: Gene expression patterns of ethanol treated and ethanol producing *Synechocystis*. Numbers of differentially regulated genes (p-value < 0.05) and expressed with (+/- 0.5), (+/- 1) and (+/- 1.5) of non-ethanologenic *Synechocystis* cultures treated with 2 %, 0.5 % and 0.05 % [v/v] ethanol after 30 min as well as non ethanologenic *Synechocystis* cultures treated with 0.5 % [v/v] ethanol after 120 min and 24 h and ethanologenic *Synechocystis* (Producer). Highest annotated hits in the corresponding range have been listed. If less than 6 genes are listed in the corresponding range it correspond to all observed changes of annotated genes.

	Producer	2 % [v/v] ethanol/30min	0.5 % [v/v] ethanol/30min	0.05 % [v/v] ethanol 30min	0.5 % [v/v] ethanol/120min	0.5 % [v/v] ethanol/24h
Differently regulated genes	**368**	**229**	**94**	**67**	**51**	**276**
Log ratio > +/- 0.5 (~ +/- 1.4 fold)	220	168	49	27 *spsA, chlG, clpP1. tgt, gltB, ccmM*	15	192
Log ratio > +/- 1 (= +/- 2 fold)	60	53	11 *htrA*	0	6 *cpcG2, mntC, htrA*	74 *psbM, nplT, uvrC, spoU, psbH, psbA*
Log ratio > +/- 1.5 (~ +/- 2.8 fold)	20 *adhA,ndhD5, mntC, cpcG2 mrp(A,C,E,F,G) cbiM, groEL1*	8 *cpcG2 pilA7*	0	0	2 *cpcG2*	13 *psbM, nplT, uvrC*

All transcriptional changes from the microarray experiments are depicted as log ratios. Overall expression pattern clearly showed a late response (24 h) of cultures treated with 0.5 % [v/v] ethanol. Significant (p-value < 0.05) changes in transcript accumulation of 94 genes in response to the exposure to 0.5 % [v/v] ethanol can be found after 30 min, 51 after 120

min and 276 after 24 h. Sorted by level of the transcript accumulation of an up or down-regulation of 0.5, the picture becomes more clear with 192 transcripts being regulated after 24 h, 16 after 120 min and 49 after 30 min with 0.5 % [v/v] ethanol. A clear difference in the overall expression pattern can be seen in the time course of one day. A strong fast reaction (30 min) and a strong late reaction (24 h) can be found. To catch the immediate response upon ethanol, the concentration used was a sub-lethal concentration of 2 % [v/v]. 2 % [v/v] ethanol was also used for further experiments. 0.05 % [v/v] ethanol was used as an ethanol concentration in which cells show no effect on growth retardation and cell viability. 0.05 % [v/v] ethanol was also the ethanol concentration in the medium of ethanologenic *Synechocystis*, under standard laboratory condition, when they were harvested. 229 transcripts have been affected significantly affected under 2 % [v/v] ethanol under which 168 transcripts were regulated above the level of 0.5 and 67 and 27 respectively at 0.05 % [v/v] ethanol. Parallel conducted experiments with *Synechocystis* cultures harboring an ethanol production cassette with a stress reacting promotor (HspA) driven expression of *Z.mobilis* pyruvat decarboxylase and the probable *Synechocystis* alcoholdehydrogenase (AdhA) (slr1192) showed 368 significantly changed genes and 220 over a level of 0.5 (cultivation done by Dr. Jan Kehr). Samples for the producer have been taken in the beginning of the production at an OD_{750} of ~1.2 as it has been the case of the other cultures used in the microarray experiments. A summary of transcription pattern can be found in Tab.1 and a complete list of significantly differentially regulated genes in the context of all annotated *Synechocystis* genes can be found in supplemental Tab.1. A similar picture was observed in literature. A comparative study on the data of different microarray experiments of different groups that analyzed the effects of ethanol on yeast showed that the affected gene categories (gene ontology categories) were similar (Stanley *et al.* 1997). Analogies to these ontology categories (Fig.5) can be found to a similar extent in the transcriptional effects *Synechocystis* exhibits after exposure to ethanol.

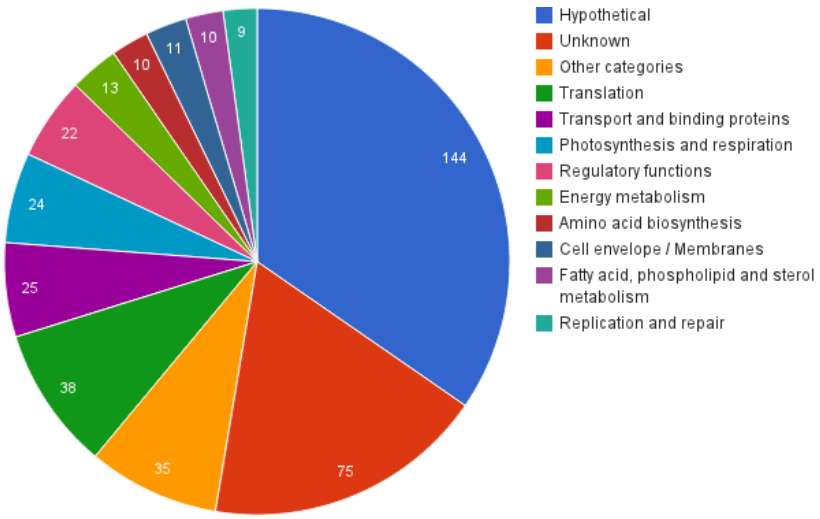

Figure 5: Differential regulated genes of ethanol dependent transcription response sorted by functional categories. Significant (p-value < 0.05) changes in transcription in microarray experiments with external ethanol.

As strong transcriptional changes stayed limited, the purpose of the detailed look into the significant changes is determining the targets of ethanol, to give an understandable background for certain phenomena and for didactical reasons. Particularly striking in its appearance with its relative high induction in multiple experimental setups was cpcG2. Together with *psbA2*, as one of the representative of the up-regulated PS II related genes after 24 h in 0.5 % [v/v] ethanol and pilA7, as a gene encoding a cell envelope located pilus with an unknown function, were selected for the verification experiments for the microarray experiments. Analyzes via Northern blotting showed all tested signals consistently to the presented microarray data (Fig.6).

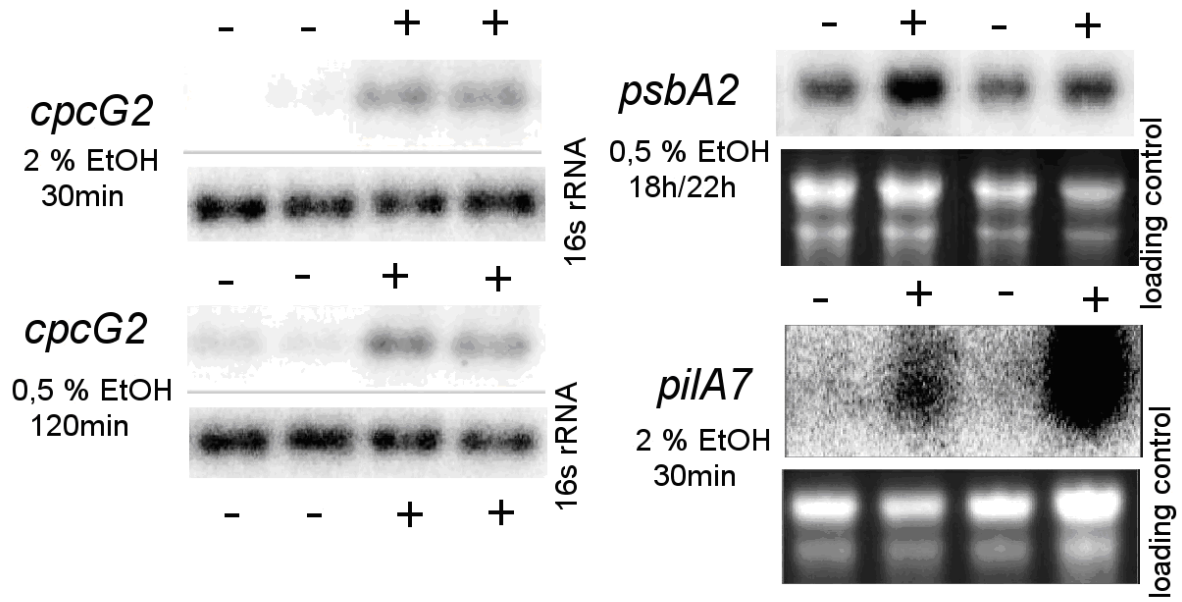

Figure 6: Northern blot verification of microarray experiments. Northern blot experiments with probes for *cpcG2*, *psbA2* and *pilA7*. Total RNA was taken from cultures with 2 % [v/v] ethanol after 30 min (*pilA7* and *cpcG2*) and from cultures with 0.5 % [v/v] ethanol after 120 min (*cpcG2*) and 18 / 22 h (*psbA2*), respectively. Each signal represents a biological replicate used for the microarray experiment (*cpcG2*, *pilA7*) and for a further control experiment (*psbA2*).

2.2.2 Functional transcriptional categories affected by ethanol

2.2.2.1 Replication and cellular DNA repair machinery associated genes

After ethanol treatment a differential effect on transcript level of genes associated with the replication process of the cells was observed. Transcriptional data indicates that *Synechocystis* cultures show signs of growth impairment already at low concentrations of ethanol (0.05 % [v/v]). A down-regulation of a variety of genes related to the cell division were found in ethanol treated *Synechocystis*. Transcripts for an *ftsH* homolog (slr1390) or *scm1* (sll1120) are two examples which can be found to be regulated. With a rising concentration of ethanol in the medium the effects become more prominent as *Synechocystis* show strong cell division problems in physiological measurements at an initial ethanol concentration of two percent (Fig.7 / Fig.8). Microarray experiments with external ethanol identified a down-regulation *ftsZ*, *ftsH3*, *ftsH4* and also *gidA* and *surE*. All represent transcripts coding for proteins which are involved in the cell division of *Synechocystis*.

Table 2: List of ethanol-affected genes with function in processes related to cell division. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30 min 0.05%[v/v] ethanol	30 min 0.5%[v/v] ethanol	30 min 2% [v/v] ethanol	120 min 0.5%[v/v] ethanol	24 h 0.5%[v/v] ethanol	function
divK 8	slr2041		-0.2				
ftsZ	sll1633			-0.54			cell division protein FtsZ
ftsH	slr1390	-0.31					cell division protein FtsH
ftsH3	slr1604					-0.78	cell division protein FtsH
ftsH4	sll1468					-1.06	cell division protein FtsH
gidA	sll0202					-0.99	glucose inhibited division protein A
surE	sll1108			-0.97			stationary-phase survival protein homolog

In more detail 0.5 % [v/v] ethanol treated cells begin with a down-regulation of transcripts coding for the cell division response regulator DivK 8 (-0.20) after 30 min and end with a down-regulation of transcripts associated with two cell division proteins FtsH (sll1468) (-1.06) and FtsH3 (slr1604) by -0.78 as well as for the glucose inhibited division protein A (sll0202) (-0.99) after 24 h. At 0.05 % [v/v] ethanol in the medium transcripts coding for another FtsH homolog (slr1390) (0.31) and the SCM1 (sll1120) (-0.43) were down-regulated. Also at the highest used concentration of 2 % [v/v] ethanol after 30 min the gene coding for SurE (sll1108) a stationary-phase survival protein homolog was down-regulated by -0.97. Also the transcript coding for the cell division protein FtsZ (sll1633) was down-regulated by -0.54.

Ethanol dependent effects on the cellular DNA repair machinery related genes of *Synechocystis* were observed. With all applied concentration of ethanol a tendency of a transcriptional reduction of this group was observed. As an example with a concentration of 2 % [v/v] ethanol and the sampling time of 30 min the transcript coding for the DNA mismatch repair

protein MutS was down-regulated by -1.33. The same occurrence was observed in 0.5 % [v/v] ethanol after 30 min with a down-regulation by –0.88. Further down-regulated candidates were in 2 % [v/v] ethanol treated cultures the gene coding for the excinuclease ABC subunit A, UvrA (slr1844) by -1.04 and transcripts of the subunits B and C (sll0459, sll0865) by -0.28 and –1.6 respectively after 24 h in 0.5% [v/v] ethanol.

Additionally several genes coding for transposases were down-regulated in 0.05 % [v/v] and 0.5 % [v/v] ethanol treated cultures. After 30 min in 0.5 % [v/v] ethanol the gene for the transposase slr1885 was down-regulated by -0.63 and after 120 min the gene coding for the transposase sll1716 by -0.20. Even at a final concentration of 0.05 % [v/v] ethanol a down-regulation of the gene coding for a transposase, namely slr1683, occurred by -0.69.

Table 3: List of ethanol-affected genes with functions in processes related to the DNA repair machinery. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30 min 0.05%[v/v] ethanol	30 min 0.5%[v/v] ethanol	30 min 2% [v/v] ethanol	120 min 0.5%[v/v] ethanol	24 h 0.5%[v/v] ethanol	function
mutS	slr1689		-0.88	-1.33			DNA mismatch repair protein
mutM	slr1689	0.45					formamidopyrimidine-DNA glycosylase
uvrA	slr1844			-1.04			excinuclease ABC subunit A
uvrB	sll0459					-0.28	excinuclease ABC subunit B
uvrC	sll0865					-1.6	excinuclease ABC subunit C
recJ	sll1354	-0.4				0.28	single-strand-DNA-specific exonuclease RecJ
recQ	slr1536					0.35	ATP-dependent DNA helicase
ruvB	sll0613				-0.18		Holliday junction DNA helicase RuvB
ssb	slr0925					0.42	single-stranded DNA-binding protein
	sll0459					-0.28	excinuclease ABC subunit B
	slr1885		-0.63				transposase
	sll1716				-0.2		transposase
	slr1683	-0.69					transposase
	ssl2789		-0.39				similar to resolvase
	sll0395					-0.5	phosphoglycerate mutase

The effects *Synechocystis* exhibits after a treatment of 0.05 % [v/v] ethanol appeared to be differentially in certain aspects to the other concentration. This can be seen for example by the observation that the gene coding for the single-strand-DNA-specific exonuclease RecJ (sll1354) appears to be down-regulated by -0.40 in 0.05 % [v/v] ethanol treated cells and up-regulation by 0.28 in cultures which were treated with 0.5 % [v/v] ethanol for 24 h. Also at the same time point transcripts for the ATP-dependent DNA helicase RecQ were accumulating by 0.35 compared to the untreated cells. Also up-regulated was at the lowest concentration mutM, a gene which is coding for the formamidopyrimidine-DNA glycosylase (slr1689) by 0.45.

2.2.2.2 Stress response upon ethanol exposure: a transcriptional difference between ethanol treated and ethanologenic *Synechocystis*

Stress response appeared on the one hand hard to put into a specific stress category group as certain genes coding for proteins which are involved cellular responses known from stress situation associated with aluminum (slr0580), iron (sll1392), arsenate (ssr1169) and bacitracin (sll0210) were affected. On the other hand certain transcript accumulation patterns were found which fitted into the proposed target groups of ethanol (Halsworth *et al.*, 1992).

Transcriptional response of stress related genes associated with salt stress condition can be seen. An enhanced transcription of a gene coding for Gcp (slr0807), a probable o-sialoglycoprotein endopeptidase where a knockout lead to reduced salt tolerance (Zuther *et al.*, 1998), and of another gene which is coding for ESI3 (ssr1169) a salt stress induced hydrophobic peptide, were observed at presence of ethanol. Also it could be seen that transcripts coding for the cell envelope associated proteases HtrA (slr1204) or ClpP1 (slr0542) which are essential for UV-B acclimatization at low temperatures (Porankiewiecz, 2002) accumulated. Like transcripts coding for the proteases HrtA which was up regulated under 0.5 % [v/v] and 2 % [v/v] ethanol another protease was up regulated after 30 min, namely Prp1, a protein which is also associated with N assimilation (Galmozzi, 2007).

Table 4: List of ethanol-affected genes with functions in miscellaneous stress responses. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30 min 0.05%[v/v] ethanol	30 min 0.5%[v/v] ethanol	30 min 2% [v/v] ethanol	120 min 0.5%[v/v] ethanol	24 h 0.5%[v/v] ethanol	function
htrA	slr1204		1.44	1.08			protease
prp1	sll2008		0.24	1.1			processing protease
gcp	slr0807	0.2		0.24			probable o-sialoglycoprotein endopeptidase
clpP1	slr0542	0.57					
clpX	sll0535					0.59	ATP-dependent Clp protease ATPase subunit
groEL1	slr2076		0.25				60kD chaperonin
dnaK1	sll0058					-0.56	DnaK protein 1. heat shock protein 70. molecular chaperone
hsp33	sll1988			-0.42			33 kDa chaperonin
	slr0580			1.07			aluminum resistance protein homolog
	sll0210	0.35				0.36	bacitracin resistance protein
sun	slr0679			0.69			sun protein
arsC	slr0946	0.47				-0.48	arsenate reductase
	ssr1169					1.17	stress induced hydrophobic peptide homolog
pfsR	sll1392			0.96		0.49	Fe homeostasis&stress-response regulator

Duo to the nature of this work and that it appears that majority of the negative effects for the cell from ethanol production are contributed by the presents of ethanol, the detailed

presentation of the microarray data are mainly focused on the transcriptional response to external ethanol. Nevertheless at certain points principle differences arises which have to be discussed. Judging the transcriptional cell response difference, between ethanologenic and ethanol treated *Synechocystis* cultures show next to the very apparent difference in a strong up-regulation of the MRP cluster in ethanologenic *Synechocystis* another remarkable feature. Ethanol treated cells showed no general stress response associated with the heat shock response. This is quite surprising as ethanol response generally seems to be associated with the heat shock response in various organisms (Bokhorst-van de Veen *et al.*, 2011; Sang-Ho-Park *et al.*, 2001). On the contrary genes coding for the heat shock protein Hsp33 and DnaK1 were down-regulated under ethanol exposure in *Synechocystis*. On the contrary ethanologenic *Synechocystis* exhibits a clear accumulation of heat shock response associated transcripts *hspA, dnaJ, grpE*. GroEL1 showed to be an interesting candidate for further analyses as its corresponding gene is differentially regulated under heat and cold stress (Kovács *et al.*, 2001) as well as under ethanologenic and ethanol treated cells (supplemental Tab.1). GroEL1 will be presented in the context of experiments of the toxic intermediate acetaldehyde (chapter 2.4.3.) later in this work. Another difference can be seen in the profile of affected genes coding for sigma factors. While ethanol treated *Synechocystis* cultures showed only a down-regulation of sigA, which was also observed under ethanologenic conditions, ethanologenic *Synechocystis* showed also a down-regulation of sigI and sigE. Subsequent Northern blot analyses with *Synechocystis* cultures treated with 2 % [v/v] ethanol for 24 h with sigD,E,F,G,H,I probes yielded no clear differences in signals. The aforementioned analyzes with acetaldehyde may also here be a contributing factor.

2.2.2.3 Miscellaneous transcription factors and synthesis related genes of amino acids and nucleotides

In other organisms it was shown that a specific composition of amino acids could enhance the ethanol tolerance. As in many organisms, also for yeast was reported (Kaino *et al.*, 2008) that prolin acts as stress protectant. Under ethanol exposure, transcripts coding for tRNA synthetases (for histidine, lysine, argenine) were down-regulated. All are alkaline amino acids and lysyl-tRNA synthetase is an interaction partner of thioredoxin (Trx) and will be discussed later in this work. In contrast to the aforementioned tRNA synthetases, transcripts coding for tRNA synthetases of proline, glycine and phenylalanine were elevated under 2 % [v/v] ethanol.

Special attention should be taken to the up-regulation in ethanol producing *Synechocystis* cells of the tryptophan synthase beta subunit (slr0543) as ethanol adapted *E. coli* highly accumulates tryptophan as reaction to 5 % [v/v] ethanol (Horinouchi *et al.* 2010). Nucleotide synthesis appeared in general down regulated with the exception of prs after 24 h in ethanol. Also apart from the transcription factors, which were discussed in this work, two further genes coding for transcript factors were found to be down regulated. The genes coding for Hik6 was down-regulated (-0.54) after 30 min and the gene coding for Rre18 was down regulated after 24 h by –0.6 at the presence of 0.5 % [v/v] ethanol. Hik6 is associated with the membrane composition under cold stress (Sugita *et al.*, 2007) and Rre18 plays a role under UV-B Stress

(Cadoret *et al.*, 2005).

Table 5: List of ethanol-affected genes with function in the synthesis of amino acids. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30 min 0.05%[v/v] ethanol	30 min 0.5%[v/v] ethanol	30 min 2% [v/v] ethanol	120 min 0.5%[v/v] ethanol	24 h 0.5%[v/v] ethanol	function
arcC	sll0573			0.81			carbamate kinase
lysS	slr1550			-0.71			lysyl-tRNA synthetase
argS	sll0502			-0.67			arginyl-tRNA-synthetase
hisS	slr0357		-0.28				histidyl-tRNA synthetase
alaS	sll0362					-0.37	alanyl-tRNA synthetase
glyS	slr0220					0.48	glycyl-tRNA synthetase beta chain
pheT	sll1553					0.49	phenylalanyl-tRNA synthetase
proS	sll1425					0.63	proline-tRNA ligase
tgt	slr0713	0.53					tRNA-guanine transglycosylase
	slr0877	0.33					glutamyl-tRNA(G) amidotransferase subunit A
gcvP	slr0293			-1.26			glycine dehydrogenase
gifB	sll1515		0.5	0.61			glutamine synthetase inactivating factor IF17
trpC	slr0546			-0.74		-0.2	indole-3-glycerol phosphate synthase
asd	slr0549			0.48			aspartate beta-semialdehyde dehydrogenese
ilvC	sll1363				-0.24		ketol-acid reductoisomerase
cynS	slr0899			-0.56			cyanate lyase
gltB	sll1502	0.52					NADH-dependent glutamate synthase large subunit

Table 6: List of ethanol-affected genes with function in the nucleotide synthesis and miscellaneous transcription factors. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30 min 0.05%[v/v] ethanol	30 min 0.5%[v/v] ethanol	30 min 2% [v/v] ethanol	120 min 0.5%[v/v] ethanol	24 h 0.5%[v/v] ethanol	function
prs	sll0469					0.89	ribose-phosphate pyrophosphokinase
purB	sll0421		-0.3	-0.89			
nrdF	slr0591			-0.61			ribonucleoside-diphosphate reductase beta chain
pyrF	sll0838			-0.34			orotidine 5' monophosphate decarboxylase
adk	sll1059					-0.81	adenylate kinase
hik6	sll1871		-0.54				
rre18	sll1624					-0.6	

2.2.2.4 Translation and transporter associated genes

External ethanol and ethanol production show strong impact on transcription accumulation of genes involved in the translational apparatus like ribosomal genes. 18 ribosomal genes have been found to be significantly affected by ethanol or ethanol production in the microarray experiments conducted from standard laboratory conditions. On the up-regulated side was the gene coding for the elongation factor EF-G (sll0830) by 0.90 which plays a role in the D1 synthesis (Kojima *et al.*, 2007). On the down-regulation side was the gene coding for the elongation factor EF-G *fusB* (sll1098) by -0.42. The observed transcriptional changes also reflecting the functionality status of the EFG based on their oxidative state (Kojima *et al.*, 2007).

Table 7: List of ethanol-affected genes with function in the translation. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30min 0.05%[v/v] ethanol	30min 0.5%[v/v] ethanol	30min 2% [v/v] ethanol	120min 0.5%[v/v] ethanol	24h 0.5%[v/v] ethanol	definition /comments
fus	sll0830			0.9		0.42	elongation factor EF-G
fus	sll1098					-0.41	elongation factor EF-G
tufA	sll1099					-0.57	elongation factor Tu
scm1	sll1120	-0.43					chromosome segregation protein
truB	slr0457	-0.46					tRNA pseudouridine synthase B
	slr1673					-1.49	prob. tRNA/rRNA methyltransferase
	slr0120					-1.2	prob.tRNA/rRNA methyltransferase
pth	slr0922					-0.11	peptidyl-tRNA hydrolase
matX	sll0927		0.34				S-adenosylmethionine synthetase
	sll1343		-0.76	-1.02			aminopeptidase
	slr1540					-0.9	mRNA-binding protein
	slr0918		0.18				methionine aminopeptidase
	sll1967	0.23					Probab. RNA methyltransferase
rpl10	sll1745					-0.48	50S ribosomal protein L10
rpl17	sll1819					-1.15	50S ribosomal protein L17
rpl18	sll1811					-1.07	50S ribosomal protein L18
rpl23	sll1801			0.47		-0.41	50S ribosomal protein L23
rps5	sll1812			-0.6			30S ribosomal protein S5
rps12	sll1096	0.38	-0.38			-0.62	30S ribosomal protein S12
rps13	sll1816			-0.62			30S ribosomal protein S13
rps18	ssr1399					0.82	30S ribosomal protein S18
rps20	ssl2233					0.47	30S ribosomal protein S20
rpl25	sll1824					1.27	50S ribosomal protein L25
rps21	ssl0601					1.1	30S ribosomal protein S21

Table 8: List of ethanol-affected genes with transporter function. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30min 0.05%[v/v] ethanol	30min 0.5%[v/v] ethanol	30min 2% [v/v] ethanol	120min 0.5%[v/v] ethanol	24h 0.5%[v/v] ethanol	definition /comments
nhaP	slr1727		-0.69	-1.12			eukaryotic Na+/H+ exchanger
	sll0993	0.46					potassium channel
	sll1428					-0.58	probable sodium-dependent transporter
ggtD	slr0531			-0.25		-0.6	glucosylglycerol transport system permease
melB	sll1374					0.57	probable sugar transporter
mntC	sll1598				1.25		Mn Transporter
coaT	slr0797					1.12	cobalt efflux pump
fecB	slr1319			0.6			iron(III) dicitrate transp. sys. substrate-binding protein
cmpB	slr0041			-0.83			bicarbonate transport system permease protein
cmpC	slr0043	0.78		-1.34			bicarbonate transport system permease protein
nrtB	sll1451			-0.57			nitrate/nitrite transport system permease protein
nrtC	slr0043	0.78				-1.34	nitrate/nitrite transport system ATP-binding protein
nrtD	sll1453					-0.95	nitrate/nitrite transport system ATP-binding protein
cysA	sll1041	-0.44	-0.3				sulfate transport ATP-binding protein CysA
	slr1229					-0.96	sulfate permease
pstA	slr1249		0.42				phosphate transport system permease protein
pstC	slr1248	0.42					phosphate transport system permease protein
	sll1481			0.34			ABC-transporter membrane fusion protein
	slr0615			0.73			ATP-binding protein of ABC transporter
	slr1149					-1.6	ATP-binding protein of ABC transporter
	slr0544					-0.29	ATP-binding protein of ABC transporter
	slr0354	-0.39					ATP-binding protein of ABC transporter
natE	slr1881			-0.43			ATP-binding subunit of the ABC-type Nat permease for neutral amino acids
secF	slr0775			-0.62			protein-export membrane protein
acrF	slr2131					-0.69	RND multidrug efflux transporter
	slr0753			0.61			probable transport protein

Analyzing the microarray data revealed an impact of ethanol on the transcript accumulations of the transport systems in and out of the cells. The gene coding for the glucosylglycerol transport system permease protein GgtD was down regulated by -0.25 and –0.6 at 2 % [v/v] (30 min) and 0.5 % [v/v] (24 h) respectively. Glucosylglycerol, a compatible solute, sustains cell division under salt stress (Ferjani *et al.*, 2003). The sheer number of ion transporters found in the microarray experiments, indicating a similarity in transcriptional cell response between ethanol and high salt treated *Synechocystis*. If it comes to transporter a dominant part can be explained by a cellular response for ion homeostasis, which can be seen i.e. in the up-regulation of phosphate (slr1948, slr1949) and potassium (sll0992) transporter and a down-regulation of sodium transporter (slr1727, sll1428). The importance of ion homeostasis upon ethanol was shown in yeast where a knockout of an ethanol induced transcriptional regulator *ETP1* plays an essential role in ethanol adaptation and activates a Na^+ ATPase (Snowden *et al.*, 2009). The transcriptional similarity ethanol and osmo stress treaded cells can be also seen in the transcription profile of some histidine kinases.

Table 9: List of ethanol-affected genes with regulatory function in the ion homeostasis. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30min 0.05%[v/v] ethanol	30min 0.5%[v/v] ethanol	30min 2% [v/v] ethanol	120min 0.5%[v/v] ethanol	24h 0.5%[v/v] ethanol	definition /comments
hik2	sll1147		-0.41			0.86	Glutathione S-transferase
hik34	slr1285		0.52				salt osmo
hik41	slr1305				-0.38		nitrogen fixation positive activator / salt und osmo
gcp	slr0807	0.2		0.24			probable o-sialoglycoprotein endopeptidase

Genes coding for Hik2 as a hyper osmotic stress induced protein (Paithoonrangsarid *et al.*, 2004) and Hik41 which is assumed to work together with additional sensory mechanisms role in salt perception (Marin, 2003) were regulated under ethanol.

Next to the down-regulation of the transcripts for the bicarbonate transporter a down-regulation of RNA levels related to the carbon dioxide concentrating mechanism was observed. The gene coding for the protein CcmK was down-regulated after 30 min in 2 % [v/v] ethanol by –0.36 and after 120 min in 0.5 % [v/v] ethanol by –0.34. Carbon, sulfur, phosphorus and nitrogen limitation are known to influence the PC content (Schwarz and Forchhammer, 2005). Whole-cell absorption spectra of *Synechocystis* will show a strong impairment with the PC upon exposure to ethanol and under ethanol production condition (chapter 2.4.2.) . The lack of transcriptional difference of N transporter and the absence of difference of NblA genes, which are needed for PC degradation under N depletion (Baier *et al.*, 2001), are indications that the ethanol dependent bleaching of *Synechocystis* is not duo limitation of macro nutrients.

Table 10: List of ethanol-affected genes with function in nitrogen and bicarbonate metabolism. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30min 0.05%[v/v] ethanol	30min 0.5%[v/v] ethanol	30min 2% [v/v] ethanol	120min 0.5%[v/v] ethanol	24h 0.5%[v/v] ethanol	definition /comments
ccmK2	sll1028			-0.36	-0.34		carbon dioxide concentrating mechanism protein CcmK
ccmM	sll1031	0.5					carbon dioxide concentrating mechanism protein CcmM, putative carboxysome structural protein
rbcS	slr0012			-0.46			ribulose bisphosphate carboxylase small subunit
ecaB	slr0051		0.17				periplasmic beta-type carbonic anhydrase
cupB	slr1302				-0.34		protein involved in constitutive low affinity CO2 uptake
prp1	sll2008		0.24	1.1			processing protease
nusA	slr0743				-0.3		N utilization substance protein
nifR3	slr0644		0.17				nitrogen regulation protein NifR3 homolog

2.2.2.5 Cell envelope lipid synthesis associated genes

Literature data proposed that external ethanol exposure is primary affecting physically structure of the cell envelope (Walker, 1998). *Synechocystis* showed up-regulation on exposure of 2 % [v/v] ethanol after 30 min of the gene coding MurE (slr0528) and after 24 h in 0.5 % [v/v] ethanol of the gene coding EnvA (sll1508) the UDP-3-0-acyl N-acetylglcosamine deacetylase, both are involved in the assembly of the peptidoglycan layer. In other organisms, transcript accumulation of pili genes as associated to external appendices were affected (Camarena *et al.*, 2010). A similar picture can be seen in *Synechocystis* where transcripts *pilI,J,L,M,A7,A10* accumulated differently under ethanol exposure.

Table 11: List of ethanol-affected genes with function associated with the cell envelope. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30min 0.05%[v/v] ethanol	30min 0.5%[v/v] ethanol	30min 2% [v/v] ethanol	120min 0.5%[v/v] ethanol	24h 0.5%[v/v] ethanol	definition /comments
murE	slr0528					0.94	UDP-N-acetylmuramoylalanyl-D-glutamate--2, 6-diaminopimelate ligase
	slr0624					0.76	UDP-N-acetylglucosamine 2-epimerase
rfbA	sll0207					-0.94	glucose-1-phosphate thymidylyltransferase
envA	sll1508			0.5			UDP-3-0-acyl N-acetylglcosamine deacetylase
	slr1424					0.22	UDP-N-acetylenolpyruvoylglucosamine reductase
	slr1962						probable extracellular solute-binding protein
pgl1	sll1568					0.26	fibrillin
pilA7	slr1930			1.6			Function unknown
pilA10	slr2016					-0.51	
pilI	slr1043					0.59	
pilJ	slr1044	0.47					methyl-accepting chemotaxis protein
pilL/cheA	slr0322		-0.31				two-component hybrid sensor and regulator /Hik43
pilM	slr1274			0.29			probable fimbrial assembly protein PilM,
pixJ2	sll0042					-0.43	

After 30 min in 0.5 % [v/v] ethanol also the gene coding for CheY, which is required for positive photo taxis (Yoshihara *et al.*, 2000) and for the signal transduction of cold stress (Suzuki *et al.*, 2000) was up regulated. Impairment with the cell membranes is a further important stress factor as ethanol per se is interacting with hydrophilic cell parts (Hallsworth, 1996). It was shown that ethanol is increasing the membrane fluidity by lowering the transition temperature of bilayers (Jain *et al.*, 1977). It was also shown that ethanol treatment leads

to an instant leaking through the bacterial cell membrane of preloaded carboxyfluorescein in *Oenococcus oeni* cells (Silveira *et al.*, 2002). Short term ethanol exposure experiments on *Vibrio parahaemolyticus* (Chiang *et al.*, 2008) and laboratory evolution experiments with ethanol on *Clostridium thermocellum* (Michael *et al.*, 2009) showed changes in the cell membrane fatty acid composition via desaturases which led to a rigidification resembling a cellular cold stress response. The conducted microarray analysis confirmed the analogy to *Synechocystis* with the down-regulation after 24 h in 0.5 % [v/v] ethanol of the desaturases coding genes desB, desD by -0.56 and -0.55 respectively.

Table 12: List of ethanol-affected genes with function associated with the lipid synthesis. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30 min 0.05%[v/v] ethanol	30 min 0.5%[v/v] ethanol	30 min 2% [v/v] ethanol	120 min 0.5%[v/v] ethanol	24 h 0.5%[v/v] ethanol	function
desB	sll1441					-0.56	acyl-lipid desaturase (omega-3)
desD	sll0262					-0.55	acyl-lipid desaturase (delta 6)
accA	sll0728			-0.33			acetyl-CoA carboxylase alpha subunit
accB	slr0435					0.44	biotin carboxyl carrier protein of acetyl-CoA carboxylase
	slr1841					0.85	probable porin; major outer membrane protein
birA	sll1655					-1.24	similar to biotin [acetyl-CoA-carboxylase] ligase
fabD	slr2023		-0.38				malonyl coenzyme A-acyl carrier protein transacylase
sqdX	slr0384				-0.09		sulfoquinovosyldiacylglycerol biosynthesis protein SqdX
shc	slr2089			-0.23			squalene-hopene-cyclase
gldA	slr1167					-0.46	glycerol dehydrogenase
	slr1916			0.72			probable esterase
hetI	slr0495			0.81			
rer1	sll0038		0.34				cold stress signal transduction

Also genes coding for the in the fatty acid synthesis involved proteins FabD (slr2023) and AccA (sll0728) were regulated after ethanol exposure. After 30 min the gene coding for AccA was down regulated by -0.33 at 2 % [v/v] ethanol and the gene coding for FabD by -0.38 at 0.5 % [v/v] ethanol. After 24 h an differential transcript accumulation for AccB the biotin carboxyl carrier protein of acetyl-CoA carboxylase (slr0435) by 0.44 and the biotin-acetyl-CoA-carboxylase-ligase BirA (sll1655) by –1.24 in 0.5 % [v/v] ethanol were observed. Also slightly down regulated were the genes coding for Shc, a squalene-hopene-cyclase, by –0.23 after 30 min in 2 % [v/v] and SqdX the sulfoquinovosyldiacylglycerol biosynthesis protein by –0.09 at 120 min in 0.5 % [v/v] ethanol respectively.

Impairment with the membrane maybe also could explains the involvement of genes coding for Hik34 in the in 2 % [v/v] ethanol treated cultures as its involvement has been shown in the cold stress response in strains of *Synechocystis* which had a genetically engineered changed membrane composition (Inaba *et al.*, 2003). Ethanol dependent impairment could

further play a bigger role in the negative effects of ethanol on *Synechocystis* cells as it was shown that the fluidity of the membrane plays also a crucial role in the adhesion of the PC proteins. This can be seen in the detachment of the PC proteins under a cold temperature shift (Ulrich *et al.*, 1979).

Protein membrane interaction which is leading to a rigidification of the membrane was proposed to be a major course of ethanol induced cell disturbance of the membranes (Grac *et al.*, 2003).

2.2.2.6 The ethanol dependent response on the photosystems of *Synechocystis* and a possible connection to energy transfer and redox associated genes

Next to the described ethanol dependent effects genes coding for proteins associated with the Chl synthesis were affected. Despite the up-regulation of one gene, slr0056, encoding the 33kd subunit of the Chl synthetase by 0.63 at the end concentration of 0.05 % [v/v] ethanol, Chl synthesis related genes had the tendency to be down-regulated. This is indicating a connection between their transcript accumulation and the later in this work presented measured Chl impairment in ethanol treated *Synechocystis* cultures (chapter 2.3.1.). After 30 min in ethanol the gene encoding for the oxygen-dependent coproporphyrinogen III oxidase HemF (Schluchter *et al.* 1997) was down-regulated with -0.49 in 0.5 % [v/v] ethanol and the gene coding for the oxygen-independent coproporphyrinogen III oxidase (sll1876) HemN was down-regulated with -0.61 at 2 % [v/v] ethanol treated cultures. Transcripts for the cobalamin synthesis protein CobW homolog slr0502 and the precorrin-6y C5, 15-methyltransferase CobL were down-regulated by -0.96 after 24 h in 0.5% [v/v] ethanol. Another aspect, the decarboxylating function of CobL, must also be taken into account in identifying the causalities of its transcriptional appearance. The gene for the iron stress Chl binding protein IsiA was up-regulated by 0.95 after 30 min in 2 % [v/v] ethanol and the gene for the billiverdin reductase (slr1784), a protein used in the phycobilliprotein sythesis (Schluchter *et al.* 1997), was down-regulated by -0.48. Also seen was an up-regulation of the gene coding for the phytoene synthase CrtB, which is involved in the synthesis of Car (Sozer *et al.* 2010), by 0.53 after 24 h in 0.5 % [v/v] ethanol. Together with the above mentioned transcriptional changes it could give an indication that ethanol treatment leads to an impairment of pigment containing elements of *Synechocystis*. Whole-cell absorption spectra (Fig.13 / Fig.15) and Car measurements I (Fig.16) of ethanol treated *Synechocystis* later in this work will draw the possible connection.

Table 13: List of ethanol-affected genes with function in processes related to chlorophyll synthesis. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30 min 0.05%[v/v] ethanol	30 min 0.5%[v/v] ethanol	30 min 2% [v/v] ethanol	120 min 0.5%[v/v] ethanol	24 h 0.5%[v/v] ethanol	function
chlG	slr0056	0.63					33kd subunit of the Chl synthetase
hemN	sll1876			-0.61			coproporphyrinogen III oxidase (O2 independent)(Schluchter *et al*. 1997)
hemF	sll1185		-0.49				coproporphyrinogen III oxidase (O2 dependent)
cobL	sll0099					-0.96	precorrin-6y C5, 15-methyltransferase /
cobW	slr0502					-0.96	cobalamin synthesis protein
crtB	slr1255					0.53	phytoene synthase
bvdR	slr1784		-0.48				billiverdin reductase
isiA	sll0247			0.95			iron-stress Chl-binding protein

The most striking effect of the microarray experiment was seen on transcripts of genes which code for the photosynthetic complexes. *CpcG2* (sll1471) coding for a phycobilisome rod-core linker polypeptide showed with an up-regulation of 3.58 or (a 12–fold) the highest induction. A similar effect could be seen in the mid term reactions after 120 min with the addition of ethanol to the final concentration of 0.5 % [v/v], where it had the second highest induction with 1.76. Also the gene coding for the transcriptional regulator Hik32/CcaS, which is known to positively regulate *CpcG2*, was up regulated under ethanol. This is further validating the importance of *CpcG2* in the transcriptional response on ethanol.

Table 14: List of ethanol-affected genes with function in the photosystems. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30 min 0.05%[v/v] ethanol	30 min 0.5%[v/v] ethanol	30 min 2% [v/v] ethanol	120 min 0.5%[v/v] ethanol	24 h 0.5%[v/v] ethanol	function
cpcG2	sll1471			3.58	1.76		phycobilisome rod-core linker polypeptide
ccaS/ hik32	sll1473		1.15				phytochrome-like sensor histidine kinase
cph/ hik35				0.88			cyanobacterial phytochrome 1. histidine kinase
apcB	slr1986					0.3	allophycocyanin beta subunit
psaD	slr0737					0.58	PS I subunit II
psaK1	ssr0390		0.51				PS I subunit X
psbZ	sll1281		-0.55				protein modulating the electron flow to PSII
PsbU	sll1194				0.34		PSII 12 kD extrinsic Protein / stability PSII (Inoue-Kashino *et al.* 2005)
psbQ	sll1638					0.86	hypothetical protein (Summerfield 2005)
psbA3	sll1867					1.34	PS II D1 protein
psbA2	slr1311					1.09	PS II D1 protein
psbT	smr0001					1.1	PS II PsbT protein
psb29	sll1414	-0.63		-0.78			hypothetical protein / involved in the PSII assembly

The gene coding for Psb29 a protein associated with the assembly of PS II (Keren *et al.*, 2005) was down regulated by -0.78 after 30 min in 2 % [v/v] ethanol and the same effect with an end concentration of 0.05 % [v/v] ethanol was observed seen in a down-regulation of -0.63. With 0.5 % [v/v] ethanol treated cells after 24 h the up-regulated site for the photosynthetic apparatus associated genes were i.e. the gene coding for the PS I subunit X (ssr0390) which can be found by up-regulated by a log-ratio difference of 0.51. Two further genes coding for the photo synthetic apparatus were slightly up regulated. PsbU the PSII 12 kD extrinsic protein which provides stability in the oxygen evolving system in PS II (Inoue-Kashino *et al.*, 2005) after 120 min by 0.34 and PsbQ (sll1638) by 0.86 after 24 h. PsbQ has a photoprotective function (Summerfield *et al.*, 2005). In general after 24 h in 0.5 % [v/v] ethanol the effect on repairing and protecting the PS becomes more eminent. With the highest induction of the experimental setup the genes coding for PsbM the PS II reaction centre M protein and, the known for it function in recovery and protection of the PS II (Bergantino *et al.* 2003), PsbH were up regulated by 2.62 and 1.35 respectively. Genes coding for PsbA3 the PS II D1 protein and also PsbA2 were on the up regulated site by 1.34

and 1.09 respectively. Also the gene coding for PsbT another component of the PS II was up regulated by 1.10.

Only two genes associated with the PS I were up regulated. One is coding the precursor of the reaction center subunit III with an induction of 0.92 and the second is for the PS I subunit I, psaD, which was up regulated by 0.58.

The up-regulation of the gene for the mangan transporter MntC (Tab.8) goes hand in hand with an up-regulation of the genes coding for the D1 protein. Additionally the gene for PsbO the PS II manganese-stabilizing polypeptide gets up-regulated after 24 h in 0.5 % [v/v] ethanol by 0.69. Mn is needed for the oxygen evolution at the D1 Protein (Bartsevich *et al.*, 1995). This is already indicating a problem with the redox status of the cells as D1 protein is the preferential target of reactive oxygen species. Also the gene coding for the glycine decarboxylase complex, represented at ethanol stress with the transcription of gcvP was down regulated. GcvP, the corresponding protein, plays a crucial role in adaptation to high light (Hackenberg *et al.*, 2009). Additional two genes which are coding for phytochrome associated histedine kinases were up regulated after 30 min. hik35 by 0.88 at 0.5 % [v/v] ethanol and hik32 by 1.15 at 2 % [v/v] ethanol.

Phycobilisomes get immobilized in glycine betaine solution (Yang *et al.*, 2007) and under high osmotic condition and therefore it was suggested that water activity around the thylakoid membrane has a major influence on the reaction centers (Kondo *et al.*, 2009). *Synechocystis* has two different phycobilisomes with a difference in their core linkers which plays an important role in the reconstitution of rods and allophycocyanins (Glickand and Zilinskas, 1982). *CpcG2* has in contrast to *CpcG1* a hydrophobic region and has a proposed non-specific interaction with the membrane on which its preference to PS I is based (Kondo *et al.*, 2009) and therefore might have different interaction properties with ethanol. *CpcG2* has also unique properties as it is associated with the PS I but gets up regulated under PS II condition (Hihara *et al.*, 2001) so it does not contradict the strong preferential up-regulation of PS II genes under ethanol treatment. Generally, the PS stoichiometry PS I / PS II ratio is redox regulated, and prolonged excess excitation of PS II versus PS I induces a higher PS stoichiometry PS I / PS II ratio and vice versa (Fujita, 1997). During state transitions *CpcG2* stays solely at the PS I (Kondo *et al.*, 2009) and therefore a possible difference in ethanol interaction could be one contributing factor for a possible ethanol dependent impairment with the state transition of *Synechocystis*. A possible impairment with the state transition of *Synechocystis* is also in accordance with fluorescence measurements which showed an immediate misbalance of the PS of ethanol treated encapsulated *Synechocystis* cells which lead to a reduced plastoquinine pool (David *et al.*, 2011) and therefore should trigger a response as it is seen in redox stressed cells. The proposed photo protective transcriptional response (David *et al.* 2011) might be seen i.e. by the up-regulation of genes coding for PsbO and PsbU. Both have their function in the protection of the PS (Summerfield *et al.*, 2007).

A few genes coding for proteins associated with the energy transfer have been found to be regulated in response to 0.5 % [v/v] ethanol after 24 h. Genes encoding for the cytochrome b6-f complex subunit PetM (smr003), which has a regulatory function in the redox state of the cells (Schneider *et al.*, 2001), as well as the response regulator for energy transfer from phycobilisomes to PS, Rre26 (slr0947), were up regulated by 0.79 and 0.70 respectively. After

30 min the transcripts for cytochrome c oxidase subunit II CtaC (sll0813) and the cytochrome b559 b subunit PsbF were also slightly up regulated. In detail ctaC was up-regulated by 0.24 at 2 % [v/v] ethanol and psbF by 0.24 at 0.5 % [v/v] ethanol.

One example of a gene, which had a reduction in transcription in all three experimental concentrations after 30 min, was sll0449 a hypothetical protein which has a postulated function to protect the photosynthetic mechanism by regenerating the oxidized form of $NADP^+$ and thereby preventing the over-reduction of the electron transport chain and the associated photodamage to PS II (Wang *et al.*, 2004). Further other energy transfer associated regulated genes were for 2 % [v/v] ethanol cytM with a down-regulation of -0.75 after 30 min as well as the gene coding for the $NADH^+$ dehydrogenase subunit NdhB by –0.58. ndhB was also down regulated after 120 min in 0.5 % [v/v] ethanol by 0.6. Also found regulated was the gene coding for the nitroreductase-like protein DrgA by -1.03 in 0.5 % [v/v] ethanol after 24 h. DrgA plays a role in the electron flow from PS I (Elanskaya *et al.*, 2004).

Table 15: List of ethanol-affected genes with function in relation to the energy transfer. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30 min 0.05%[v/v] ethanol	30 min 0.5%[v/v] ethanol	30 min 2% [v/v] ethanol	120 min 0.5%[v/v] ethanol	24 h 0.5%[v/v] ethanol	function
petF, fdx	slr0150				1.1		ferredoxin, petF-like protein
isiB	Sll0248					-0.6	flavodoxin
rre26	slr0947		0.08			0.7	response regul. for energy transfer from PC tops
cytM	sll1245			-0.75			cytochrome cM
ctaC	sll0813			0.21			cytochrome c oxidase subunit II
psbF	smr0006				0.24		cytochrome b559 b subunit
cbaB	sll1869					0.09	Prob. dioxygenase, Rieske iron-sulfur component
drgA	slr1719					-1.03	nitroreductase-like protein / role in the electron flow from PSI (Elanskaya *et al*. 2004)
ndhB	sll0223			-0.58	-0.6		NADH dehydrogenase subunit 2
menA	slr1518					0.45	phylloquinone biosynthesis protein
hoxU	sll1223		-0.38	0.31			diaphorase subunit of the bidirectional hydrogenase
hoxY	sll1224					-0.63	hydrogenase subunit of the bidirectional hydrogenase
rre33	sll0797			-0.53			redox-responsive and/or Ni(II)-responsive regulator
hik14	slr1759				-0.56		redox
	sll0449	-0.41	-0.6	-0.78			unknown protein
petM	smr003					0,79	cytochrome b6-f complex subunit

With the goal to minimize the stress cells exhibit under ethanol exposure and therefore for ethanol production the cellular redox response posing a good target for optimization of the synthetic organism. The possibility of an imbalance of reductions equivalents from the photosynthetic apparatus plus the observation that ethanol causing a general imbalanced of equivalents in the TCA cycle that triggers a cellular redox response in yeast (Stanley *et al.*, 1997, Chandler *et al.*, 2009) indicating that the impairment with reduction equivalents is a major cause in the ethanol response.

Table 16: List of ethanol-affected genes with coding proteins associated with thioredoxin modulated processes. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30 min 0.05%[v/v] ethanol	30 min 0.5%[v/v] ethanol	30 min 2% [v/v] ethanol	120 min 0.5%[v/v] ethanol	24 h 0.5%[v/v] ethanol	function
trxA	slr0623					0.93	thioredoxin
tpx	sll0755					-1.02	thioredoxin peroxidase
fdx	slr0150					1.1	ferredoxin
ftrC	sll0554					1.19	ferredoxin-thioredoxin reductase, catalytic chain
eno	slr0752		1.03				enolase
glgA	sll1393					-1.1	glycogen (starch) synthase
fusB	sll1098			-0.42			elongation factor EF-G
	slr1934			-0.75			pyruvate dehydrogenase E1 component
purB	sll0421		-0.3	-0.89			adenylosuccinate lyase
gmd	sll1212			-0.97			GDP-D-mannose dehydratase
rpiA	slr0194			-0.91			ribose 5-phosphate isomerase
tufA	sll1099					-0.59	protein synthesis elongation factor
gltB	sll1502	0.52					glutamate synthase (ferredoxin)
lysS	slr1550			-0.71			lysyl-tRNA synthetase
ccmM	sll1031	0.5					carbon dioxide concentrating mechanism protein

Under ethanol exposure genes coding for proteins which are associated with the Trx and ferredoxin pathways appeared to be up-regulated. In *Synechocystis* Trx plays a major role in reducing photosynthetic produced reduction equivalents and is regulated by the electron transport chain (Navaro *et al.*, 1996). NADPH-Trx reductase pathway is important for the antioxidant system and ferredoxin-Trx reductase pathway plays an important role in the control of cell growth rate (Hishiya, 2008) and therefore could play a role in the observed reduction of transcripts concerning the cell division. Under ethanol exposure both pathways were relatively strong up regulated after 24 h. After 24 h hours with 0.5 % [v/v] ethanol an elevation of transcripts of Trx (*trxA*) by 0.93, ferredoxin (*fdx*) by 1.19 and the ferredoxin-thioredoxin reductase, catalytic chain (*ftrC*) by 1.19 was observed. 2-DE gel analysis showed a number of Trx interaction partners (Perez-Perez *et al.*, 2006) under which nearly all can be found affected directly or indirectly, as related enzymes in their pathways, by exposure to ethanol. Under the potential trx targets first and foremost *cpcB* can be found which was also strongly differentially expressed under pervious conducted production experiments (Fig.4B).

A possible indirect relation was seen in the down-regulation of the gene coding for the alpha chain (slr1934) by –0.75 after 24 h in 0.5 % [v/v] ethanol and the gene coding for the beta chain (sll1721) by –0.75 after 30 min in 2 % [v/v] of the pyruvate dehydrogenase component E1. The pyruvate dehydrogenase E2 subunit is the Trx target. Another indirect reaction where fructose-1.6-bisphosphatealdolase *FbaA* is the Trx target protein and gene

coding for the fructose 1.6-bisphosphatase II Glx gets regulated. Glx is the next enzyme after *FbaA* in the pathway. *FbaA* was also found to be constantly down regulated under production condition (Fig.4B). Also found down regulated Trx target are gene coding for the lysyl-tRNA synthetase which was already mentioned above. More examples which can be found are a down-regulation of the gene encoding the argininosuccinatelyase purB by -0.3 at 0.5 % [v/v] ethanol and by -0.89 at 2 % [v/v] ethanol. After 30 min, an up-regulation of the gene encoding the glycolysis involved protein Eno in 0.5 % [v/v] ethanol by 1.03 and a down-regulation of the gene coding glycogenphosphorylase GlgA by -1.1 after 24 h occurred. Additionally at 2 % [v/v] ethanol after 30 min the gene coding for the phosphoribulokinase RpiA was up regulated by 0.91.

Summarized it can be said that genes which are coding for proteins in Trx related processes play a major in the ethanol dependent transcriptional response. The difference in transcript accumulation of the gene encoding for *FbaA* (Fig.4) under ethanol production condition indicating that Trx related processes also play a role in the cellular response of ethanologenic *Synechocystis*. Also the observed accumulation of glycogen in ethanologenic *Synechocystis* (Fig.3) could be in connection with Trx modulated processes. Indication for this could be the above mentioned regulation of the gene coding for GlgA. Further Trx modulated processes could also play a role in the potential down-regulation of the translation seen in chapter 2.2.4. and with further various parts of the energy metabolism of *Synechocystis* presented bellow.

Ethanol leads to a down-regulation of the gene coding the enolase Eno and the gene coding the phosphofructokinase PfkA at 2 % [v/v] ethanol after 30 min by -1.04 and –0.51 respectively. Also at 2 % [v/v] ethanol after 30 min the the transcripts for the ribose 5-phosphate isomerase RpiA and the GDP-mannose 4,6-dehydratase Gmd as well as the GTP pyrophosphokinase SpoT were down-regulated by –0.93, -0.97 and –0.54 respectively.

Table 17: List of ethanol-affected genes with coding proteins associated with various parts of the energy metabolism. Changes in transcript levels depict in the absolute values of log-fold changes. Negative log-folds correspond to down-regulation. (> +/- 0.5 is ~ +/- 1.4 fold, > +/- 1 equals +/- 2 fold > +/- 1.5 is ~ +/- 2.8 fold)

GEN	ID	30min 0.05%[v/v] ethanol	30min 0.5%[v/v] ethanol	30min 2% [v/v] ethanol	120min 0.5%[v/v] ethanol	24h 0.5%[v/v] ethanol	definition /comments
pdhA	slr1934		-0.75				pyruvate dehydrogenase E1 component, alpha subunit
pdhB	sll1721					-0.56	pyruvate dehydrogenase E1 component, beta subunit
acs	sll0542					-0.29	acetyl-coenzyme A synthetase
eno	slr0752			-1.04			enolase
pfkA	sll0745			-0.51			phosphofructokinase
pgm	slr1945		-0.4			-0.92	2,3-bisphosphoglycerate-independent phosphoglycerate mutase
rpiA	slr0194			-0.93			ribose 5-phosphate isomerase
gmd	sll1212			-0.97			GDP-mannose 4,6-dehydratase
spp	slr0953					-0.9	sucrose-phosphate phosphatase
spsA	sll0045	-0.97					sucrose phosphate synthase
galE	slr1078					-0.47	similar to UDP-glucose 4-epimerase
icd	slr1289					-0.67	isocitrate dehydrogenase (NADP+)
spoT	slr1325			-0.54			GTP pyrophosphokinase
glgA	sll1393					-1.09	glycogen (starch) synthase
	slr1943		0.23				probable glycosyltransferase

After 24 h in ethanol the genes coding for the acetyl-coenzyme A synthetase Acs, the 2,3-bisphosphoglycerate-independent phosphoglycerate mutase Pgm and the sucrose-phosphate phosphatase, Spp, were down-regulated by -0.29, -0.92 and –0.9 respectively. The effects after 24 h in ethanol are further a down-regulation of genes coding for the, in the TCA cycle involved, protein isocitrate dehydrogenase Icd and and the glycogen (starch) synthase GlgA by –0.67 and -1.09 respectively. The gene coding for the pyruvate dehydrogenase E1 component, beta subunit PdhB exhibits after 24 h a down-regulation and the gene for the pyruvate dehydrogenase E1 component, alpha subunit PdhA after 30 min by –0.56 and -0.75 respectively. After 30 min a down-regulation, as seen similar after 24 h where it get down regulated by -0.92, the gene coding for Pgm gets down-regulated by –0.4. The only up-regulated gene in this category is coding for a probable glycosyltransferase (slr1943) and get up-regulated by 0.23 after 30 min in 0,5 % [v/v] ethanol. Even the at the lowest concentration in the medium of 0.05 % [v/v] ethanol a down-regulation of the gene coding for the sucrose phosphate synthase SpsA by –0.97 was observed. At ethanol exposure glycolysis related transcripts, respresented with *eno, pgm* and *pfkA*, as well the sugar metabolism related genes, represented with *rpiA, gmd, spp, spsA* and *galE*, were down-regulated. Also transcripts which are negatively regulated under ethanol exposure were one from the TCA cycle, *icd*, the transcript for the acetyl-coenzyme A synthetase, acs, as well as transcripts of the, already above as Trx targets mentioned, sub units of the pyruvate dehydrogenase *E1, pdhA* and *pdhB*.

A possible explanation for these observed phenomena is proposed in the following. The PC linker Cpg2 showed to be strongly up-regulated at the beginning of ethanol exposure. One possible consequence could be that *CpcG2* which solely binds to PSI has attachment problems with the membrane during ethanol exposure. This could lead to over reduction of the plastoquinone pool. A reduction of the plastoquinone pool as reaction to ethanol was also shown in florescence meassurements of the PS (David *et al.* 2011). The up-regulation of the PS II genes might be in the same connection. Subsequently the cells might try to perform a state transition to rebalance the exciting energy which might gets impaired by the properties of *CpcG2*. As a consequence the energy metabolism could be misbalanced and the above mentioned glycolysis genes get down-regulated after 30 min in 2 % [v/v] ethanol. Also the down-regulation of sucrose- and glycogen-related genes occurred. The above mentioned connection of Trx to genes of this category could play an essential role. Another aspect which might play a role is an interconnection between pyruvat and the ion homeostasis. *Arthrospira maxima* cells for example compensating artificial sodium gradients by increasing the energy conversion via the carbohydrate catabolism (Carrieri *et al.*, 2011).

2.3 Physiological consequences of ethanol exposure

2.3.1 Growth and chlorophyll measurements of ethanol treated *Synechocystis* cultures

To validate the effects of ethanol, a seven-day long-term ethanol exposure experiment was conducted (Fig.7) and the effects were described. In the experiment the cultures started with an ethanol concentration of 2 % [v/v] and after 7 days ended due evaporation with a concentration of 0.5 % [v/v], which resembled the state-of-the-art optimized ethanol production yield reached in this study (chapter 2.1.1.).

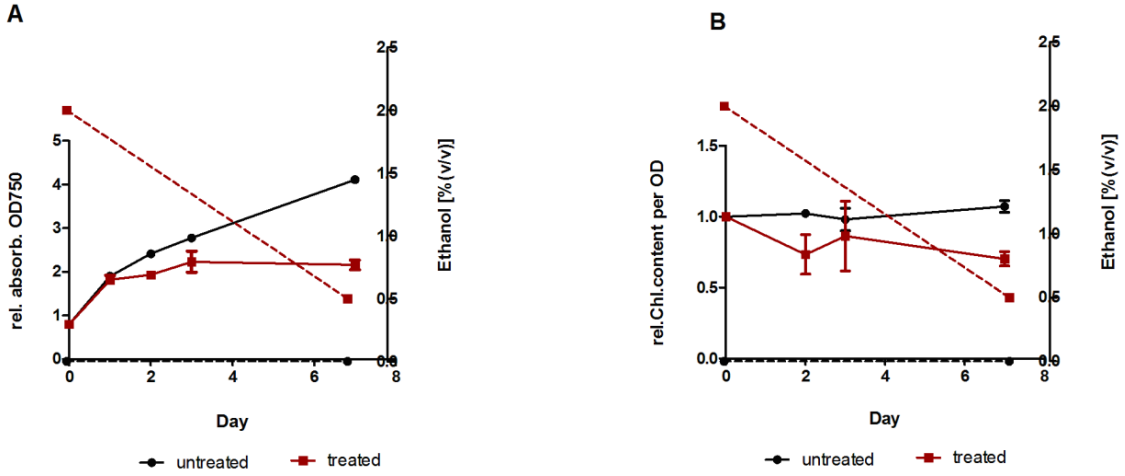

Figure 7: Growth properties and chlorophyll content of ethanol treated *Synechocystis*. Growth properties under standard laboratory conditions measured by optical densities (A) and relative Chl *a* content of ethanol treated cultures (squares) and untreated control group (circles), depicted with the ethanol concentration in the medium of ethanol treated cultures (dotted line). Each data point represents the mean of biological duplicates and double measurements. The error bars denote standard deviations.

Ethanol exposure leads to retardation of cell reproductivity and cell viability. After one day, when the growth properties stayed relatively unchanged compared to untreated cultures, the cultures exhibited a strong retardation of the cell reproductivity. This can be already seen on day 3 and 4 and even stronger at day 7 with a steeper growth curve and higher end cell count of the untreated cells (Fig.7A). The Chl content of untreated *Synechocystis* was always higher compared to *Synechocystis* treated with 2 % [v/v] ethanol (Fig. 7B).

2.3.2 Elevating ethanol tolerance

Ethanol showed to have impairment with cellular process on multiple levels (Stanley *et al.* 1997). The fundamental question must be posed if it is possible to encounter such a systemic stress in *Synechocystis*. To address this question, *Synechocystis* cultures of the previously

described experiment (chapter 2.3.1.) have been diluted to OD_{750} 0.8 and the ethanol concentration was re-adjusted to 2 % [v/v] in a repeatable manner for around 3 months. This way an adaptation to the experimental condition through serial culture directed laboratory evolution was achieved. The same was done with a concentration of 1 %. After 11 rounds / weeks the cultures have been analyzed and compared to the WT (Fig.8). The strains have been termed for further use as *Synechocystis* PCC6803-JL1 (JL1) and *Synechocystis* PCC6803-JL2 (JL2) respectively.

Directed laboratory evolution via serial culture experiments revealed that a pre-adaptation to an experimental environment including ethanol concentrations up to 2 % [v/v] (Fig.4) leads to an enhanced tolerance towards ethanol as demonstrated by the reduced retardation of the cell growth *Synechocystis* exhibits after ethanol treatment (Fig.6). Thus, it is possible to achieve an elevated tolerance of *Synechocystis* towards ethanol. Under both tested non-lethal ethanol concentrations in the medium (1 % [v/v] and 2 % [v/v] ethanol), the pre-adapted strains outperformed the WT with respect to growth in ethanol-spiked media. JL2 performed slightly better than JL1 and was used for further analyses. At 1 % [v/v] ethanol in the media, JL2 cultures already clearly outperformed the WT and JL1 cultures. At 2 % [v/v] ethanol in the medium, JL1 and JL2 exhibit only a slight decrease of the growth rate while WT cultures showed a clear retardation of growth. 5 % [v/v] ethanol in the media completely inhibited growth of all cultures and seems to exceed the adaptation capacity of *Synechocystis* cultures under this laboratory conditions and the given time frame.

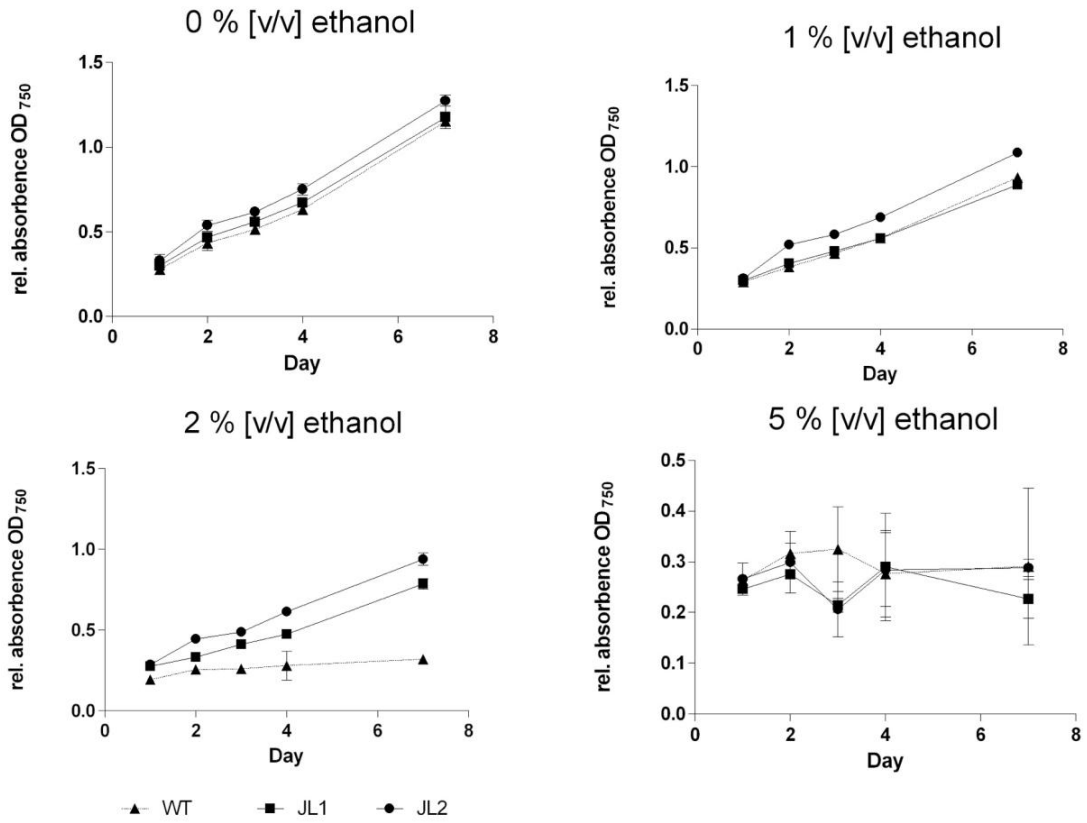

Figure 8: Comparison of growth properties at various (0 %, 1 %, 2 % and 5 % [v/v]) ethanol concentrations of *Synechocystis* cultures and *Synechocystis* cultures with a pre-adaptation to the laboratory environment. Squares represent *Synechocystis* cultures with a pre-adaptation to the laboratory environment with ethanol concentration ranging from 2 % [v/v] to 0.5 % [v/v] (JL2) and a pre-adaptation to an ethanol maxima of 1 % [v/v] (JL1) compared to the WT depicted in triangles. Experiments were performed in 100 ml Erlenmeyer flask, 40 ml culture, continuous light of about 40 μE $m^{-2}s^{-1}$ and mild shaking. Each data point represents the mean of biological triplicates. The error bars denote standard deviations.

2.3.3 Quick test for ethanol-adapted *Synechocystis* cultures

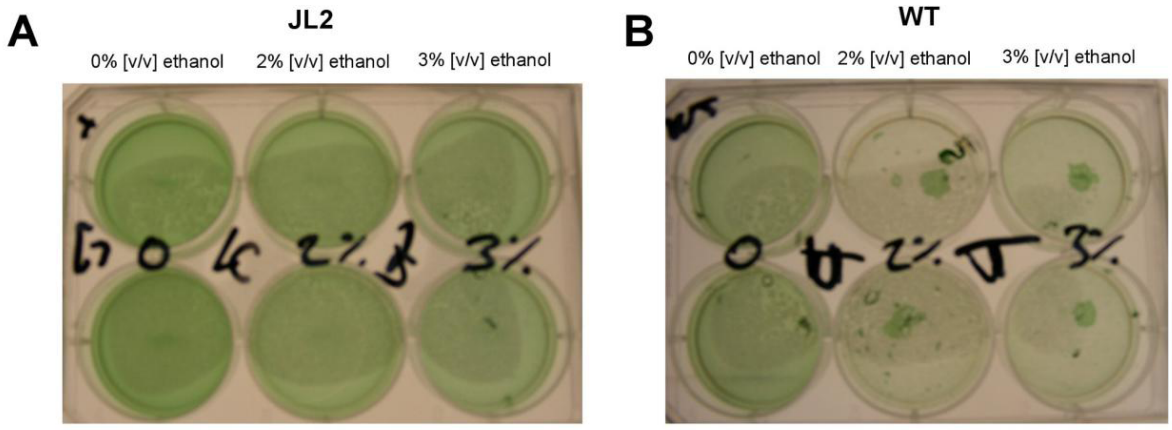

Figure 9: Quick test reference picture for distinguishing between WT and JL2. JL2 (A) and WT (B) under 0 % [v/v], 2 % [v/v] and 3 % [v/v] ethanol in six-well plates with 5 mL cultures held under ~ 40 μE m^{-2} s^{-1} light and mild shaking after an incubation period of 24 h.

In order to distinguish between JL2 strains and WT for ongoing experiments a quick test system for the cultures has been established. Before starting a new experiment, a time frame of seven days, in which no ethanol was in the medium, was held. New experiments with ethanol adapted strains started with a standardized quick test in which JL2 cultures were compared to the WT. The test is based on a 24 h stress experiment in which the different stains were spiked with different ethanol concentration in 6-well plates with a 5 mL culture volume. The results were evaluated visually compared to a reference (Fig.9). Growth analysis in 6-well plates showed a clear visual difference at the different tested concentrations of ethanol. With 2 % [v/v] ethanol treated WT *Synechocystis* cultures exhibit, in contrast to JL2 cultures, a strong agglomeration effect, which became stronger at a concentration of 3 % [v/v] ethanol in the media. At this concentration, JL2 cells started to exhibit a slightly similar effect. All cultures exhibited increasing growth retardation with rising ethanol concentrations. All these factors have been used as a confirmation before the experiments. Ethanol adapted *Synechocystis* appeared to have different sedimentation properties (Fig.9), generally a marker for impairment with pili, and thus slightly backing the observation of the impairment of ethanol with pili like structures. In order to pin point a change of ethanol adaptation PilA7 was analyzed on the Northern blot level. No significant difference between JL2 and WT cultures after the treatment with 2 % [v/v] ethanol (data not shown) was observed, validating the impairment of ethanol with the corresponding gene for PilA7 but giving no further information concerning the sedimentation property differences. The observed agglomeration of *Synechocystis* cultures in 6-well-plates after ethanol treatment (Fig.9) could further highlight the ethanol dependent impairment on cellular appendices.

2.3.4 Properties of an ethanol-adapted strain under production condition

In order to determine, whether an elevated tolerance against ethanol leads to an increased ethanol production, cultures of pre-adapted *Synechocystis*, which show the desired attitude (JL2) were conjugated with the ethanol production construct (chapter 3.2.6.4.) and compared to the corresponding WT control strain (Fig.10). The growth advances to WT of the JL2 strains under external ethanol (Fig.8) can be also be seen under ethanologenic conditions (Fig.10A). After 24 h the growth superiority of JL2 producer compared to a WT producer is already visible and increases successively with the onset of the time. The comparison study revealed that JL2 strains which are used as the production platform for ethanol showed further favorably attributes. Ethanologenic JL2 strains showed an elevated Chl *a* content under all tested time points and conditions, and further generated more ethanol. A relative percentile surplus (Fig.10B) of Chl *a* content of ethanologenic JL2 producer strains was observed. It shows a constant elevation with slight decrease in the first four days of ethanol production. The effect gets successively more visible and vivid with the onset of the production time and reaching over 60 % of the level of the ethanologenic WT strain. Parallel conducted control experiments with non- ethanologenic JL2 strains compared to a WT strain with no ethanol in the media showed a constant Chl *a* content under the same conditions and with 2 % [v/v] ethanol in the media, like in ethanologenic conditions, a higher Chl *a* content of JL2 was observed (data not shown). In the first days, the Chl *a* content surplus is comparable between non-ethanologenic conditions and ethanologenic conditions and increases successively on a prolonged time frame reaching the highest point of the experiment up to nearly 100 % surplus of the Chl *a* content of the compared WT. Ethanol measurements in media of ethanologenic cultures depicted an increased ethanol production under the tested conditions, which reached a relative percentile production surplus of over 150 % of the JL2 strain. It can be stated that a pre-adaptation to laboratory conditions and ethanol containing media leads to a significant increase in ethanol production under unchanged cultivation conditions.

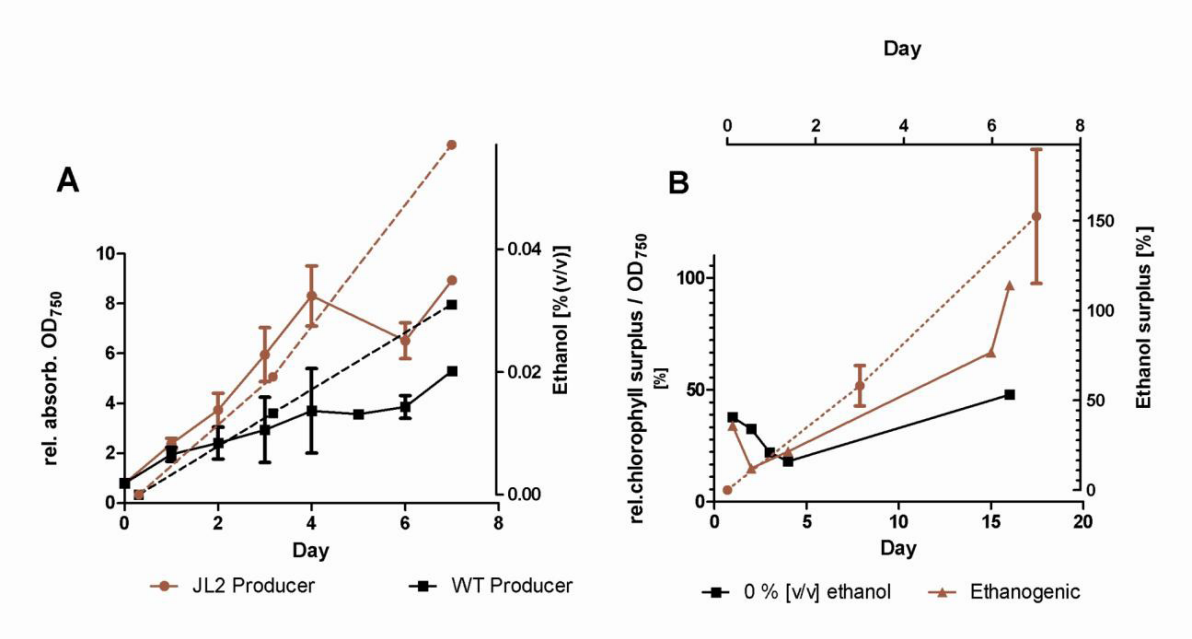

Figure 10: Growth properties and relative percentile surplus of Chl *a* content and ethanol generation of ethanologenic JL2 strain compared to an ethanologenic *Synechocystis* strain derived from a WT. Comparison of growth properties (A) of pre-adapted ethanologenic *Synechocystis* strains (JL2) (circles) vs. ethanologenic WT (squares) via optical density measurements at 750 nm (OD_{750}) and relative percentile surplus of Chl *a* (B) content of ethanologenic cultures (triangles) and non-ethanologenic cultures (squares) depict with the relative ethanol production surplus of JL2 to WT in dotted lines. The error bars denote standard deviations of duplicates under standard laboratory conditions.

2.3.5 Properties of an ethanol-adapted strain under high salinity conditions

High salt stress experiments with an increasing concentration of sea salts have been conducted (Fig.10). Under expected up-scaled production environment, conditions can change due to evaporation in the direction of higher salinity. Also, the question if acquired tolerance towards one stress (ethanol) can lead to new effects in other stress conditions (high salt stress) was addressed.

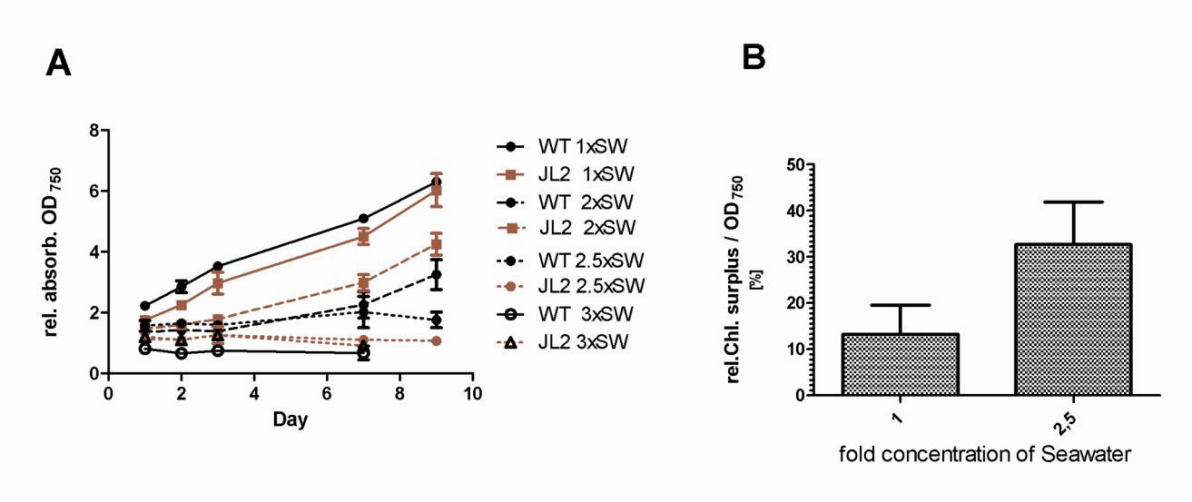

Figure 11: Growth properties (A) and relative Chl *a* content surplus in percent on day 9 (B) of pre-adapted *Synechocystis* cultures (JL2) compared to WT cultures. Circles mark WT, squares JL2 cultures. Seawater salts concentrations are depict by solid lines for 1 fold seawater concentration, big dotted lines for 2 fold of seawater concentration, small dotted lines for 2,5 fold of seawater concentration and solid lines with empty symbols for 3 fold of seawater concentration denotate as 1xSW, 2xSW, 2,5xSW and 3xSW respectively. The error bars denotate standard deviations of duplicates under standard laboratory conditions with 40 mL Erlenmeyer flasks.

Although JL2 cultures showed no clear growth advantages in higher salt concentrations, but rather show a salt concentration specific growth change compared to the WT (Fig.11A), the observed phenotype under ethanol stress with its elevated Chl *a* content cannot only be seen under the former tested condition but is manifesting also with rising salt concentrations (Fig.11B). The experiment also indicated that both used strains are very tolerant to high salt conditions and can at least survive under high salt stress with 2.5 fold seawater salts for 9 days. All in all high salinity experiments are indicating that the observed phenotype of JL2 is seen under different condition and that both stresses bear similarities to each other.

2.4 Impairment of ethanol with the pigment composition of *Synechocystis*

2.4.1 External ethanol influences the pigment composition of *Synechocystis*

External ethanol leads to clear changes in the pigment compositions of *Synechocystis*. Spectral analyses of ethanol treated cells showed an absorption patterns with a fast decrease of PC absorption and, to lesser extend, a decrease in the Chl *a* absorption. Whole-cell absorption spectra of ethanol treated *Synechocystis* cultures confirmed the decrease in Chl *a* content as observed in the Chl *a* measurements of ethanol treated cells. Also a decrease of PC absorption was detected. In accordance to described absorption peaks (Barber, 1987) ethanol

treated *Synechocystis* cultures show a steady decrease of the Chl *a* absorption at ~680 nm and the PC absorption at ~620 nm. Already 24 h (Fig.12) after the inoculation with 2 % [v/v] ethanol, a decrease of Chl *a* and the PC absorption can be seen with a marginal higher decrease of the PC absorption. After 48 h (B) and 72 h (C) these effects became stronger with PC absorption on the same level as the Chl *a* absorption on day 3. After seven days (D), the PC absorption decreased to a very low level, smaller than the Chl *a* absorption. Also a change in the carotenoid (Car) content can be observed in the spectra.

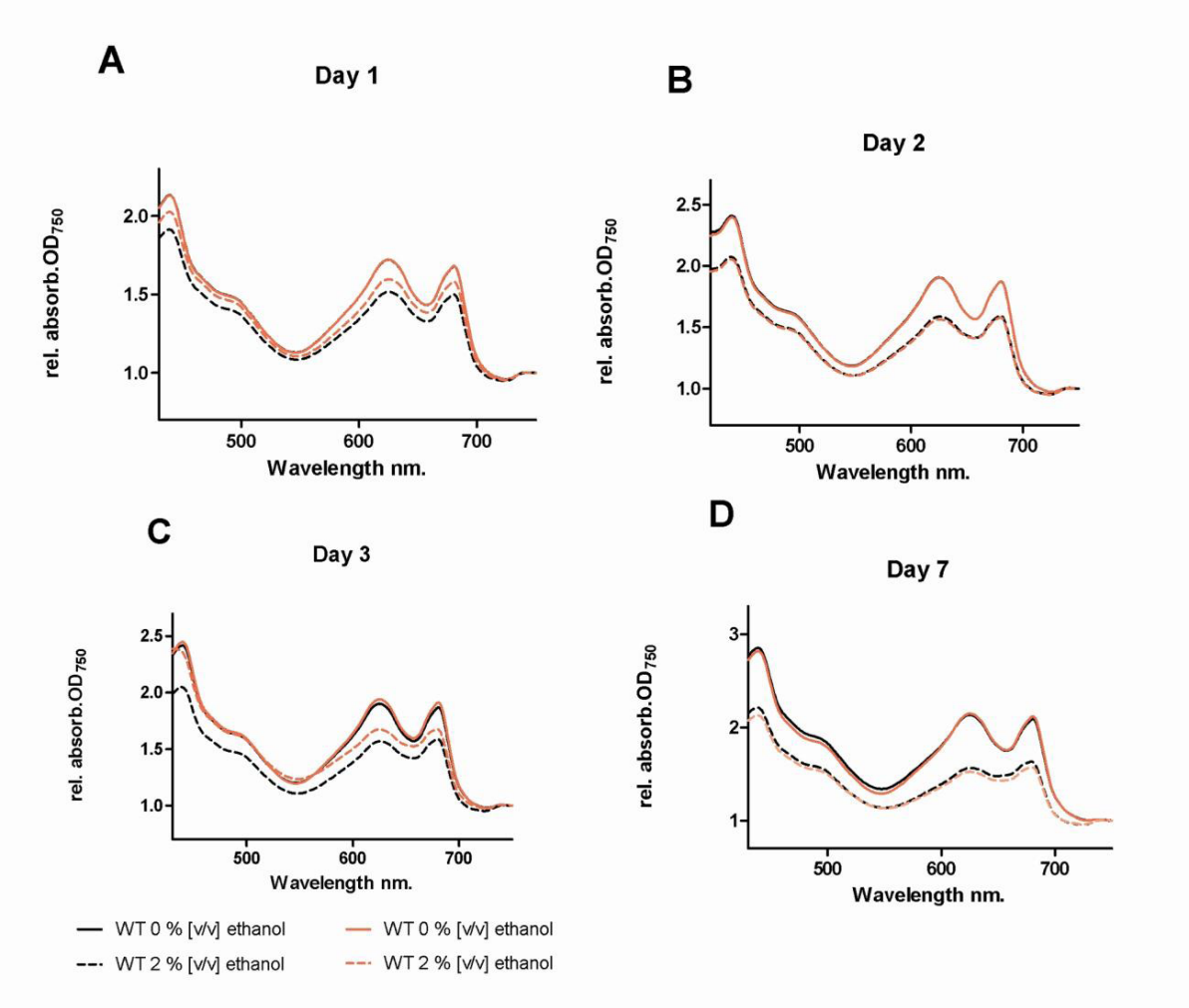

Figure 12: Whole-cell absorption spectra of ethanol treated *Synechocystis*. Whole-cell absorption spectra of ethanol treated as well as non-treated *Synechocystis* cultures with a start inoculation of 2 % [v/v] ethanol. Four representative spectra were measured: day 1 (A), day 2 (B), day 3 (C) and day 7 (D). Solid lines represent untreated cultures dotted lines represent cultures treated with ethanol. Black and red lines represent two different biological replicas.

2.4.2 The pigment composition of pre-adapted *Synechocystis* under ethanologenic and ethanol treatment conditions

The loss of Chl *a* content as well as the surplus of Chl *a* content under ethanologenic and external ethanol conditions of JL2 is also reflected in whole-cell absorption spectra analyzes, in which WT and JL2 were monitored in parallel under ethanologenic and ethanol treatment conditions with 2 % [v/v]. Whole-cell absorption spectra of parallel monitored JL2 cultures under ethanologenic and non-ethanologenic as well as on external ethanol conditions show an elevated Chl *a* absorption at ~680 nm under all tested conditions compared to the WT (Fig.13B). The greatest difference between the Chl *a* absorptions can be seen under treatment with 2 % [v/v] ethanol in which already after two days WT cultures dramatically decreased their Chl *a* absorption while JL2 cultures kept their Chl *a* absorption level relatively constant. The PC at absorption at ~620 nm in JL2 exhibits a similar decrease as in the WT under external ethanol treatment (Fig.13B), in which both strains show approximately the same PC absorption area under the peak during the first days (day 2 and day 3). After two weeks (Fig.13B,D) the PC absorption of the JL2 strain regenerates to higher levels as well as the Chl *a* absorption, while WT strains keep only basal level of the absorption. The similar picture can be observed at ethanologenic conditions. The strong decrease in the Chl *a* and PC absorption validate a decrease in cell viability under ethanol treatment and ethanol production of *Synechocystis* WT cultures. Under ethanologenic conditions (Fig.13B,A,D) JL2 cultures exhibit a more stable PC absorption. Further JL2 and WT strain exhibited a clear change in other pigment-containing elements under ethanol treatment and ethanologenic conditions.

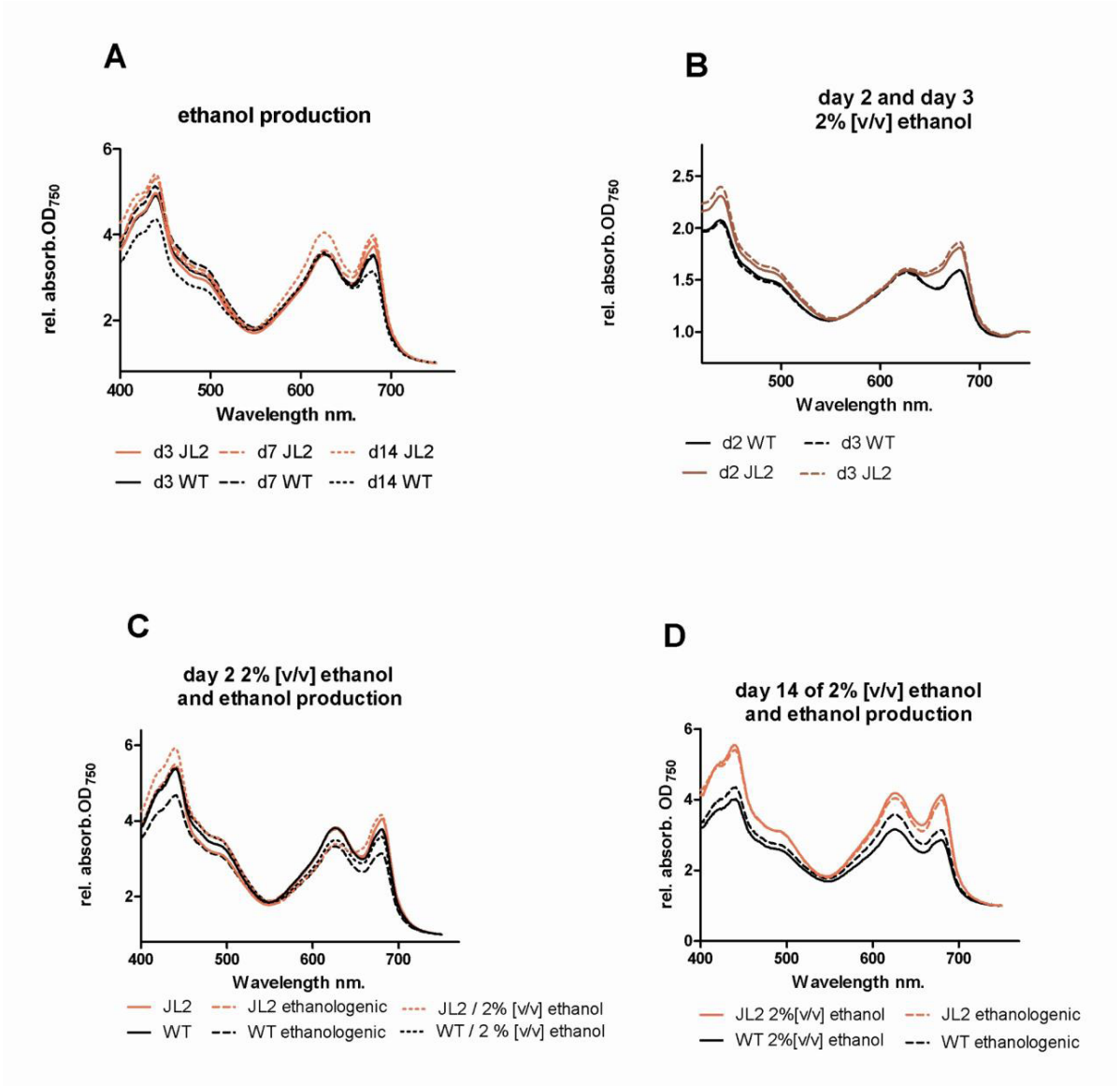

Figure 13: Whole-cell absorption spectra of ethanol treated and ethanol producing *Synechocystis*. Whole-cell absorption spectra of pre-adapted *Synechocystis* (JL2) cultures (red) compared to WT cultures (black) under ethanologenic ((A), (C), (D)) and external ethanol conditions ((B), (C), (D)). Diagram (A) marks three representative time points after the induction of the ethanol production at day 3, 7 and 14, depicted as filled, dotted and small dotted lines respectively. Diagram (B) shows whole-cell absorption spectra of *Synechocystis* treated with 2 % [v/v] ethanol at day 2 and 3, solid and dotted lines respectively. (C) and (D) show ethanologenic *Synechocystis* compared to *Synechocystis* under external ethanol condition. Ethanologenic strains are depicted in dotted lines, compared to external ethanol conditions, depicted in small dotted lines at day 2 (C) and filled lines at day 14 (D) and the untreated and non-ethanologenic WT at day 2 (solid lines). Cultivation was done in standard laboratory condition as duplicates.

2.4.3 Whole-cell absorption spectra of high salt stress treated pre adapted *Synechocystis* cultures

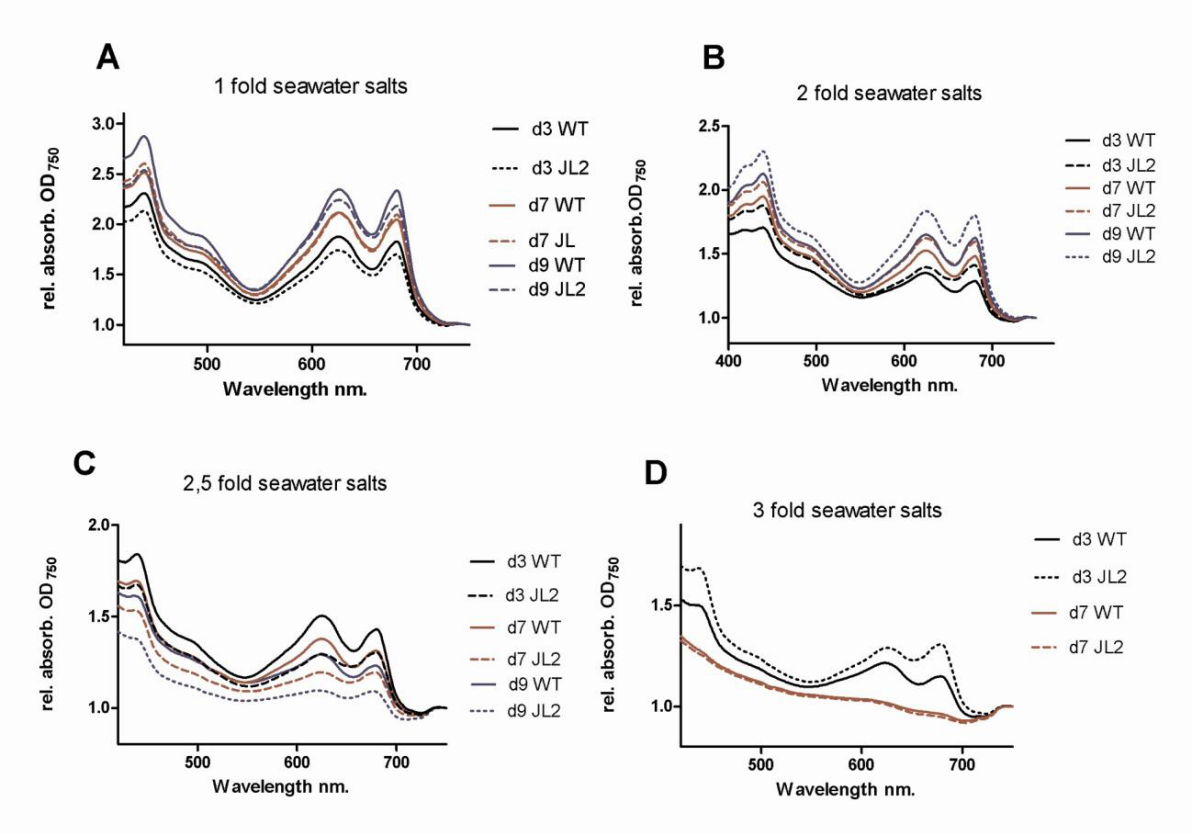

Figure 14: Whole-cell absorption spectra of *Synechocystis* under different high salinity conditions. Whole-cell absorption spectra high salt stress treated JL2 *Synechocystis* cultures marked in dotted lines compared to WT strain depicted in solid lines under four rising seawater salt concentration from 1 fold (A), 2 fold (B), 2.5 fold (C) to 3 fold (D) on up to 3 representative days marked in different colors from black (day 3), red (day 7) to blue (day 9).

For further analyzes of the observed elevated Chl *a* content in JL2 strain under various high salinity conditions whole cell absorption spectra were measured. JL2 culture showed a different picture on the reaction of high salinity with respect to pigment-contents. JL2 doesn't have the sharp decline in the Chl *a* absorption which the WT is experiencing. This picture is similar of what could be observed under external ethanol and ethanol production conditions. Comparison of the whole-cell spectra of all different tested stress conditions showed a stabilized Chl *a* absorption (Fig.14), while the difference of PC absorption between JL2 and WT in the spectra is varying from stress to stress.

Cross stress experiments with salt stress showed that under salt stress the WT is drastically loosing Chl *a* continent while ethanol adapted strains have a stable Chl *a* absorption (Fig.14) indicating that under long time adaptation to ethanol salt stress resistance plays an important role.

2.4.4 Whole-cell absorption spectra of highly controlled ethanologenic *Synechocystis*

Also in optimized reactors the loss in Chl *a* content is reflected in whole-cell absorbance spectra of ethanologenic cultures compared to the control strain (Fig.15) with a steady decrease of the Chl *a* absorption at ~680 nm.

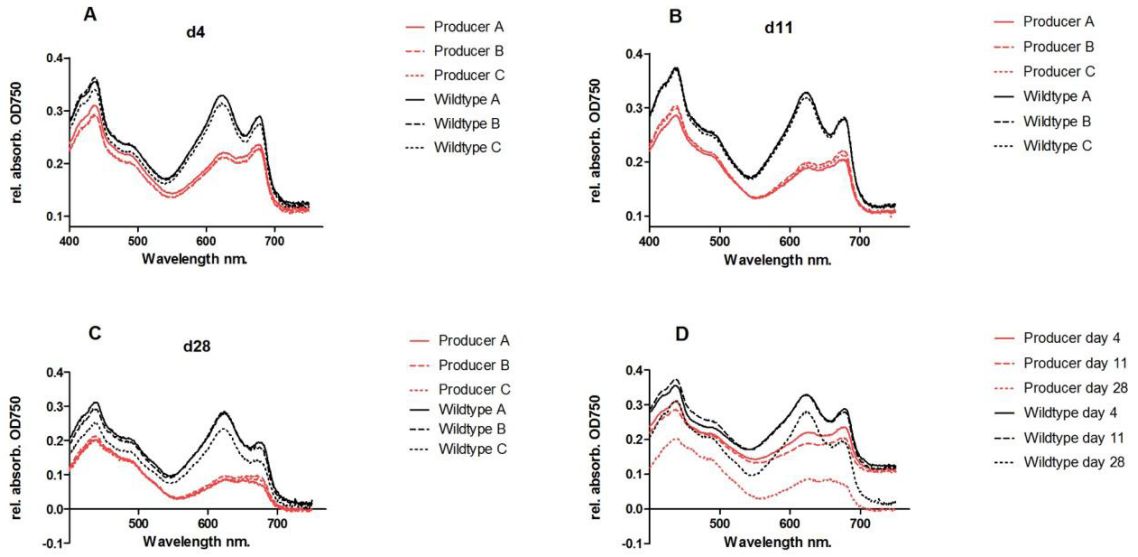

Figure 15: Whole-cell absorption spectra of producing and non-producing *Synechocystis* cultures. Spectra are taken on day 4 (A), day 11 (B), day 28 (C) and as a representation of a mixed chart on the time frame of the experiment (D).

Fig.15 reflecting the course of events *Synechocystis* cultures goes through the production of ethanol. In the starting phase of the experiment at day 4 (Fig.15A), a sharp and dramatic decline of the PC absorption at ~620 nm can be observed, while the Chl *a* absorption at ~680 nm stays relatively stable compared to the control strain. This is also reflected in the taken Chl *a* measurements (Fig.3B). At day 11 (Fig.18B) PC seemed to decrease to a marginal level, the Chl *a* absorption also begins to decline. Furthermore, a clear change in Car absorption at ~450-520 nm can be observed. By the end of the experiment (Fig.18C), (after 4 weeks of ethanol production) the Chl *a* absorption at ~680 nm also declines to a marginal level and completely decreases the cell viability of the cultures.

2.4.5 Carotenoid contents of ethanologenic *Synechocystis*

Car content analyses by HPLC were done by Cyanobiofuels GmbH. Car were determined at the beginning (day 4) and at the end (day 18) of the experiment in which a successive accumulation of a difference between the Car species (Fig.16) of ethanol producing cultures compared to the control strain can be observed.

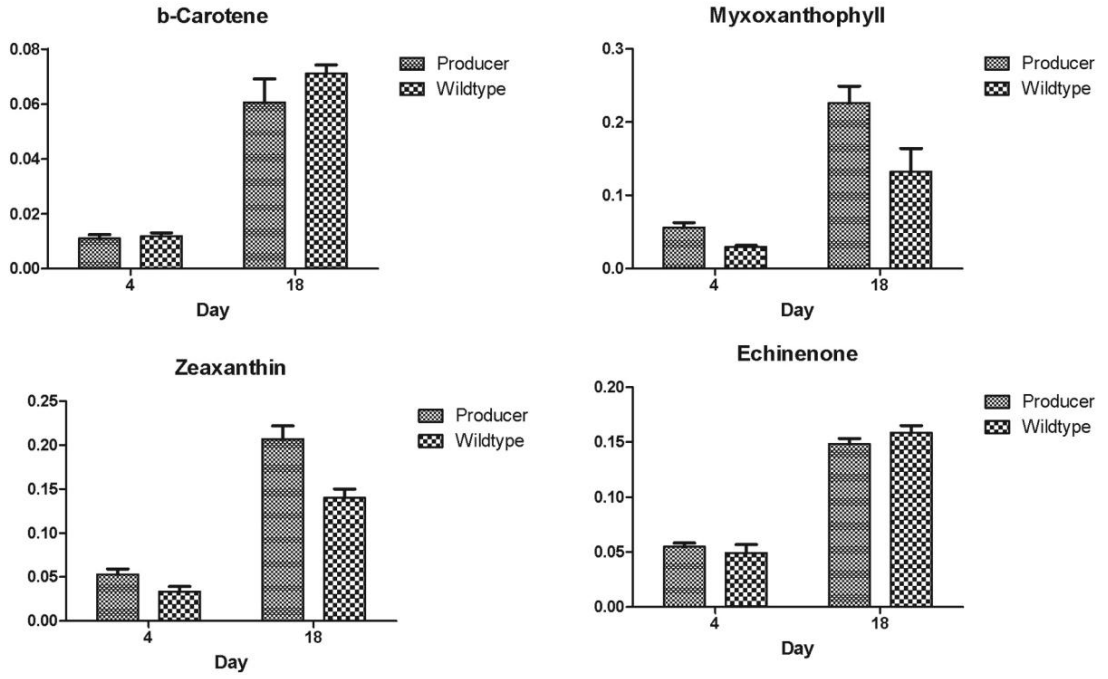

Figure 16: HPLC analyses of specific carotenoid contents of ethanologenic *Synechocystis*. HPLC analyses of specific Car content of ethanologenic *Synechocystis*. Specific Car content from cultures of ethanologenic (Producer) and non-producing (WT) *Synechocystis* cultures in optimized photo bioreactor after 4 and 18 days.

HPLC measurements of the Car content revealed that ethanologenic *Synechocystis* cultures accumulated myxoxantophyll and zeaxanthin selectively in a high manner while β-carotene and echinenone stay at a comparable level to the control strain. The effect is already vivid at the beginning of the ethanol production after four days and gets prominent in the late phase of the production at day 18. In general a decreasing Car content is a sign of a break down of the photosynthesis but was also observed to accumulate differentially under cold stress (Kłodawska *et al.*, 2012).

2.4.6 Phycocyanin subunits transcripts after ethanol production and ethanol exposure

Whole-cell spectral analyses of ethnologic *Synechocystis* revealed fundamental changes in PC content with a dramatic decrease of the PC absorption at ~620 nm (Fig.15). Accordingly, subsequent transcriptional analyses by Northern blotting of the main PC operon (*cpcBAC2C1D*) revealed a lower abundance of the functional bi-cistronic transcript *cpcBA* (~1500 nt in length) while a new specific band termed as *cpcA+* arose.

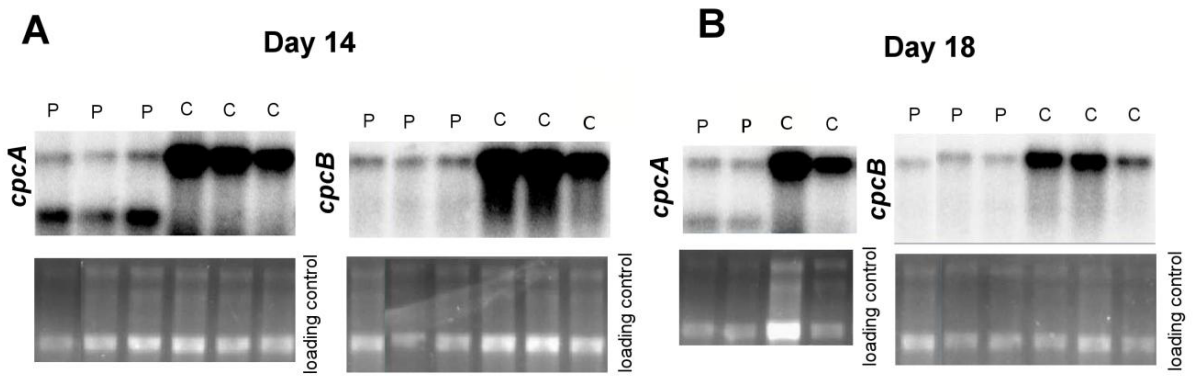

Figure 17: Northern blot analyses of phycocyanin subunits *cpcB* and *cpcA* in long term ethanologenic conditions. Northern blot analyses of cpcA and *cpcB* accumulation in an ethanol producing strain (P) of *Synechocystis*, compared to control cultures (C). Samples from two representative days at the late phase of the ethanol production (day 14 (A); day 18 (B)) 500 ng total RNA marked as loading control.

To further investigate the origin of observed signal pattern probes of different parts of the main PC operon (*cpcBAC2C1D*) were used to pin point the consistence of the fetched transcriptional signal.

Under standard laboratory conditions *Synechocystis* cultures which were exposed to an ethanol concentration of 2 % [v/v] showed the unique *cpcA*+ signal (Fig.18). The signal is at least consisting of the approximately 2/3, from the 3' part on, of a *cpcA* transcript. Probes for other genes of the operon as *cpcB, cpcC1, cpcC2* and *cpcD*, showed a similar picture as the 5' *cpcA* probe and further confirming this specific observation (data not shown). One good advantage taken from the Northern blot method is that by analyzing the hybridization bands a specific new signal appeared. This phenomenon might play a crucial role in explaining the fundamental PC loss or also just be the visual consequence of it. It also may find a good use as a biotechnological marker for ethanol presence in the medium.

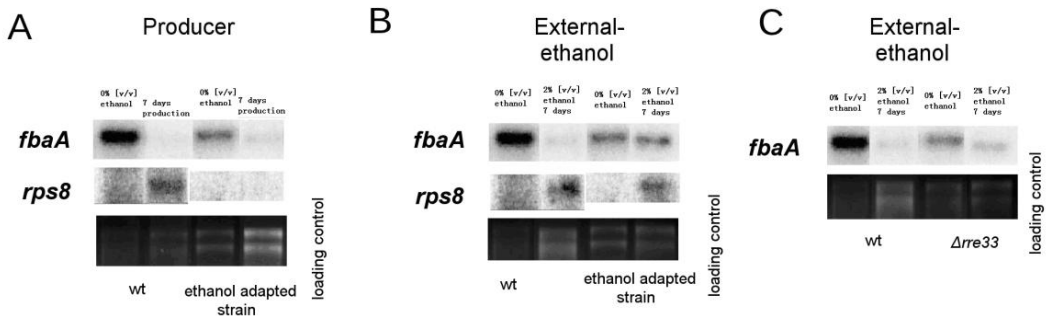

Figure 18: Northern blot analyses of the first part of the phycocyanin operon (*cpcBAC2C1D*). Schematic display of the genomic region of the *cpcBA* co-transcript (green) (A), the localization of three different *cpcA* probes (blue) (A) and the corresponding Northern blot analyses (B) after 72 h of exposure to 2 % [v/v] ethanol under standard laboratory condition. 1 μg of total RNA and was used for every lane and blotted on a nylon membrane.

From the physiological data generated for this work and the transcriptional data received from the microarray it can be concluded that ethanol production (Fig.3) as well as ethanol treatment (Fig.7) leads to a dramatic decrease in cell reproductivity and cell viability seen in the Chl *a* content and in Northern blot analyses of the PC sub unit *cpcA* (Fig.17 / Fig. 18) as well as in spectral analyses (Fig.12). *Synechocystis* cultures exposed to external ethanol exhibit a decrease in the *cpcBA* co-transcript with a rise of a new *cpcA+* transcript in optimized photo bioreactors as well as under standard laboratory.

2.4.7 Northern blot analyses with ethanol adapted and Δrre33 *Synechocystis* strains

Microarray and Northern blot analyses of ethanologenic *Synechocystis* cultures (Fig.4) show a clear down-regulation of *FbaA, ApcE, CpcB*, all are interaction partners of Trx (Perez-Perez, 2006). Northern blot analyses of long term ethanol exposed *Synechocystis* cultures (Fig.18) showing the same picture leaving the observed effect in ethanologenic *Synechocystis* to prolonged exposure to ethanol. Further a slightly different transcriptional picture of ethanol adapted and Δrre33 *Synechocystis* cultures on transcript accumulation of *fbaA* occurred.

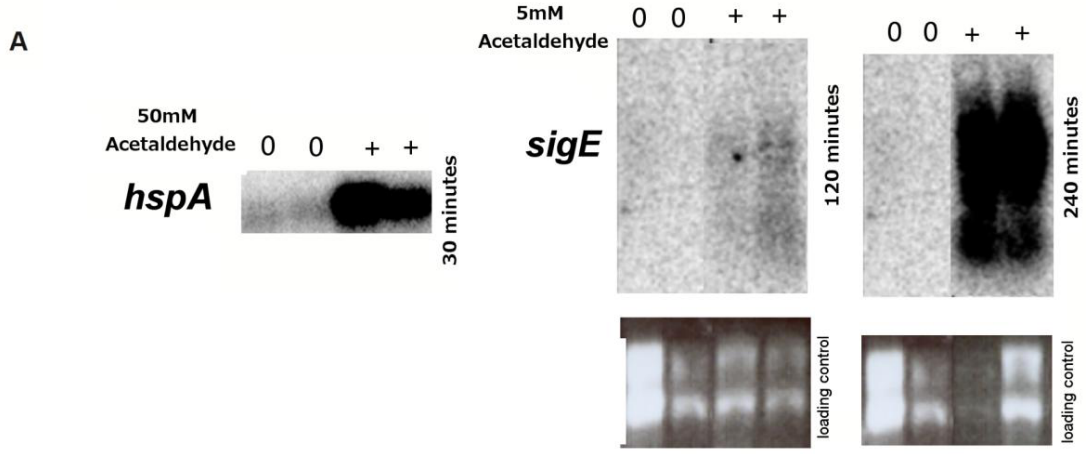

Figure 19: Northern blot analyses of ethanologenic WT and JL2 strain and WT, JL2 and Δrre33 under external ethanol condition. (A) shows Northern blot analyses of transcript accumulation *fbaA* and *rps8* of pre adapted (ethanol adapted strain) and non pre adapted (WT) ethanologenic *Synechocystis* cultures under standard laboratory condition and (B) under exposure to 2 % [v/v] ethanol. (C) shows the transcript accumulation of *fbaA* of Δrre33 compared to the WT under exposure to 2 % [v/v]. All samples were parallel taken and blotted on one membrane at day 7 after the induction of ethanol production or the inoculation with ethanol. Loading control exert corresponds to the *fbaA* signals.

Rre33 as one important regulator in redox response of *Synechocystis* (Li and Sherman, 2000) and the pre adapted JL2 strain were closer analyzed in order to validate their involvement in the ethanol response in certain genes of *Synechocystis*. Two examples of genes, *fbaA* and *rps8*, which have been found regulated under ethanologenic condition in the optimized photobioreactor, have been chosen for analysis by Northern blotting. Both genes were found to be affected not only by ethanol production but also under exposure to ethanol. Also it was shown that the effect is transferable between experimental conditions as the same pictures are seen under optimized photobioreactor and standard laboratory conditions. To check if a pre adaptation leads to a different transcriptional response in these genes and if the response regulator Δrre3 plays a role in the transcription response to ethanol, parallel experiments with ethanologenic JL2 and non ethanologenic JL2 and Δrre33 cultures with an inoculation with external ethanol have been conducted. Both JL2 and Δrre33 appeared to have an elevated base level of *fbaA* and an elevated level of *fbaA* transcripts in ethanol treated JL2 cultures compared to the ethanol treated WT occured. The elevated signal of *rps8* is only seen in JL2 cultures treated with external ethanol and not under the ethanologenic cultures under standard laboratory conditions.

2.5 External acetaldehyde

2.5.1 Differentially regulated transcriptional response of sigma factors and heat shock associated genes under acetaldehyde

As the fermentive pathway for ethanol production includes the formation of the intermediate acetaldehyde, catalyzed by pyruvate decarboxylase (PDC). Acetaldehyde is a highly toxic metabolite (Woutersen *et al.* 1986). Its toxicity and effects on transcript accumulation as a contributing factor in the ethanol production was examined. Preliminary experiments were performed in 50 mL falcon test tubes, which have been sealed to avoid gas exchange with the ambient. Within the time frame of one week all tested concentrations (0.5 mM, 5 mM and 50 mM) of acetaldehyde turned out to be lethal while non-treated *Synechocystis* cultures can survive for months in a closed 50 mL falcon tubes (data not shown). Analyzes of transcript accumulation were performed with samples from cultures grown in a sealed room under standard laboratory environment in a 24 h time frame. Sample times were 30 min, 120 min and 24 h. For the analysis, probes for the sigma factors D,E,F,G,H,I as well as heat shock protein HspA and GroEL1 were used. Gobal transcriptional analyzes GroEL1 had differential expression between ethanologenic and external ethanol conditions. All significant signal differences which were detected by Northern blot analyses are described below. As it was observed with external ethanol an immediate and time delayed transcription response was observed.

2.5.2 Short- to mid-term transcription response of genes coding for hspA and sigE after treatment with acetaldehyde

Synechocystis cultures treated with external acetaldehyde showed fast (30 min) and mid-term (120 min – 240 min) transcription responses to high concentrations of 50 mM and 5 mM acetaldehyde, respectively (Fig.20). Northern blot analyzes indicated that with 50 mM acetaldehyde in the medium transcripts of the gene coding for the stress marker of *hspA* is getting strongly up regulated (Fig.20). From these results it can be assumed that for the production of ethanol the *hspA* promotor is a suitable method for a production with a feedback loop in which the produced acetaldehyde is driving the transcription of the production cassette. With a concentration of 5 mM, an increasing transcript accumulation of *sigE* can be seen from 120 min to 240 min.

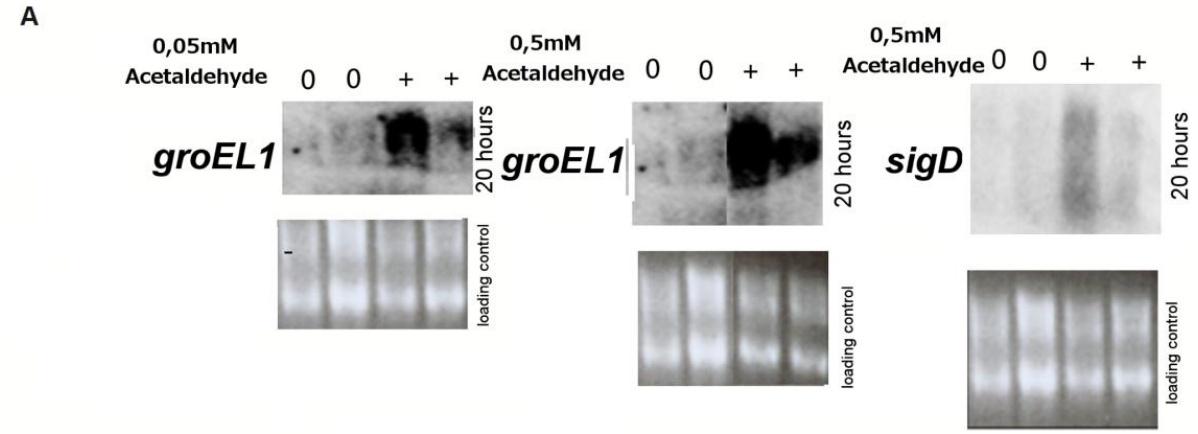

Figure 20: Northern blot analyses of the fast and mid-term response on reaction to acetaldehyde treatment in *Synechocystis*. *Synechocystis* cultures treated with 50 mM and 5 mM acetaldehyde (+) in comparison to an untreated control culture (0) under standard laboratory conditions and different time points. Total RNA were taken after 30, 120 and 240 min after the treatment with acetaldehyde and 5 μg was used for every lane and blotted on a nylon membrane.

2.5.3 Long-term transcription response of genes coding for groEL1 and sigD after treatment with acetaldehyde

The time-delayed transcription response after the treatment with acetaldehyde becomes more obvious with lower concentrations of 0.05 mM and 0.5 mM acetaldehyde, which lead to a transcription response of *Synechocystis* after 20 h (Fig.21).

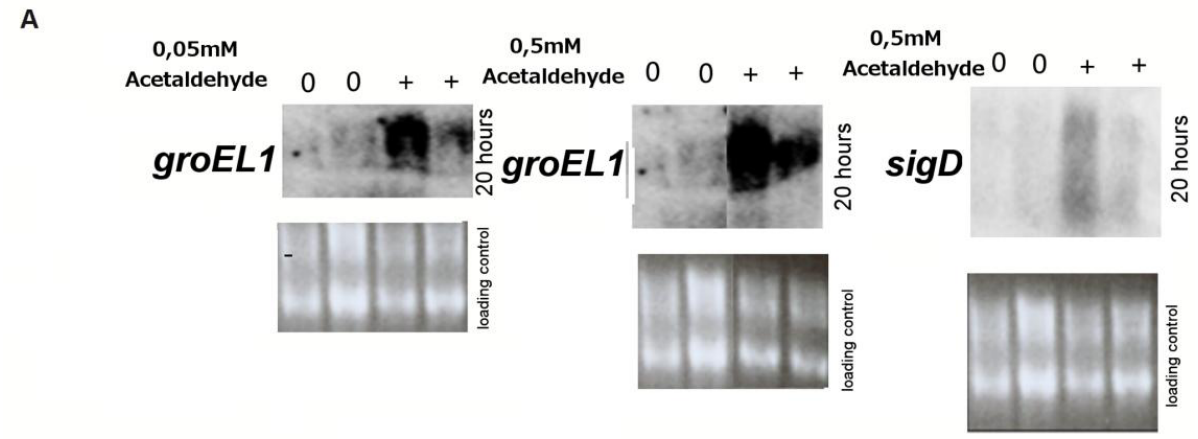

Figure 21: Northern blot analyses of the late response on reaction to acetaldehyde treatment in *Synechocystis*. Northern blot analyses of *Synechocystis* cultures treated with 0.05 mM and 0.5 mM acetaldehyde (+) in comparison to untreated control cultures (0) under standard laboratory conditions and different time points. After 20 h with acetaldehyde in the medium total RNA were taken and 5 μg was used for every lane and blotted on a nylon membrane.

As an example Northern blot analyses showed an increasing transcript accumulation of the chaperonine GroEL1 with an increasing acetaldehyde concentration from 0.05 mM to 0.5 mM after 20 h. *Synechocystis* culture treated with 0.5 mM acetaldehyde indicated an elevated transcript accumulation of sigma factor D (*sigD*) after 20 h. The late up-regulation of *groEL1* might have its reason in an accumulation of ethanol from metabolized acetaldehyde as it could resemble the up-regulation in ethanol treated cells.

2.5.4 Acetaldehyde as a possible contributing course of the observed transcriptional difference in ethanol treated and ethanol producing *Synechocystis*

The observed transcriptional difference of ethanol treated and ethanologenic *Synechocystis* of transcripts of genes coding for SigE as well as HspA may have its reason in the presence of intracellular acetaldehyde in ethanologenic *Synechocystis*. It is also possible that after 20 h most of the acetaldehyde had evaporated and part of it may have been metabolized to ethanol and therefore explaining the up-regulation of *groEL1*, as an up-regulation was also indicated in transcriptional data from ethanol treated cultures in this work and was observed in cold stress treated cultures in literature (Kovács *et al.*, 2001). Also, if part of the transcriptional difference in ethanologenic and ethanol treated *Synechocystis* could be explained by the presence of intra cellular acetaldehyde, it would mean that enzymatic reaction from acetaldehyde to ethanol lies mainly on the site of the ethanol. Two observations about the main alcohol dehydrogenase AdhA are favoring such a hypothesis. AdhA has superior catalytic efficiency for aldehyde reduction compared to that for alcohol oxidation (Vidal *et al.*, 2009) and an insertion knockout did not show significant growth inhibition difference to the WT under external ethanol conditions (data not shown).

2.6 Final discussion

Ethanol is posing systemic stress to all organisms (Halsworth, 1992). It is unlikely that cyanobacteria encounter growth inhibiting concentrations of ethanol in their natural environment, and thus the transcriptional response of *Synechocystis* on ethanol is also unlikely to be strong and specific. Ethanol showed to have a rather gradual and successive retarding effect on the reproductivity and cell viability of ethanol producing and long term ethanol treated *Synechocystis* cultures. Under external ethanol conditions strong transcriptional changes stayed limited to a few genes. Mainly the cyanobacterial antenna composition showed to be relatively strongly affected which reflected the strong decrease of the PC peak in photo spectrometric measurements of ethanol exposed cultures as well ethanol producing cultures. With all applied concentration of ethanol and all used time points transcripts coding for proteins associated with the PS have been affected. Transcriptional data indicates that ethanol impairs the utilization of light and hampers the state transition. The prominent transcriptional appearance of Trx related transcripts and preferentially up-regulated genes coding for components of the PSII shown in ethanologenic and ethanol treated *Synechocystis* illustrated this conclusion. Subsequent this might also reflect the observation of an increased number of affected genes over the time at 0.5 % [v/v] ethanol and the similarity of the transcriptional answer after 24 h to the one of 2 % [v/v] ethanol treated cells after 30 min. Higher concentration of ethanol with a possible stronger impairment with the PS might reflect the effects of the accumulation over the time of the lower concentration. These prolonged effects from ethanol exposure itself might be the reason that all by Northern blot analyzed transcripts of ethanol producing *Synechocystis* can be also found affected in the same direction by ethanol treatment with 2 % [v/v] ethanol.

Since the ethanol-producing or –treated cultures only slowly decay it is most likely that the negative effects of ethanol are also rather indirect and that an accumulation of the effects leads to the growth retardation. The rather low amplitude of transcript changes and the differences of cell response over the time reflect this observation. Functional analyzes showed an overlap in transcriptional cell responses between the different applied concentrations and different time points. In general it should be kept in mind that transcriptional data obtained from microarray experiments must be taken with caution as first not much can be said about transcription of specific genes which do not give a signal and second data of transcription do not reflect protein levels and therefore at best indicate the changes the organisms really exhibits. As ethanol from its physiological properties is by nature interacting with multiple targets in biological cells, the accumulating effect of ethanol was not surprisingly accompanied by a composition of different cell responses. The transcriptional changes showed analogies to the response of other organisms to ethanol. Sorted according to the function of the genes found in literature affected by ethanol the transcription data posed a good backing for the physiological data gained in this work. The importance of the influence of ethanol on the different functional categories was also showcased by the observation that stress experiments with high salinities and ethanol adapted *Synechocystis* show similarities in the phenotypes of ethanol stress. Adaptation to ethanol might yield several advantages. First it showed to increase ethanol production and an elevated tolerance towards ethanol. This acquired elevated

tolerance towards ethanol means also a reduction against the selective pressure against the ethanol production cassette. With a prolonged adaptation experiment it would be in theory also possible that the cells changed certain components in a way they might function better under ethanol pressure, and therefore would pose a valid attempt to raise the stability of the production. Also sequencing the adapted organism would pose a possibility to identify working resistance mechanisms against ethanol as well it could provide vital information for the road to a stable production.

3 Materials and Methods

3.1 Materials

3.1.1 Chemicals and Providers

Chemicals used in this study were purchased from Biozym, Merck, Carl Roth, Serva and Sigma-Aldrich unless specified otherwise. Ultrapure water was obtained using a USF Purelab Plus system. Sterilization of solutions and inactivation of genetically modified material was done for 20 min at 120° C / 55 kPa using a Varioklav 75 S steam sterilizer (Thermo Scientific).

Table 18: List of providers.

Ambion, Applied Biosystems ,Invitrogen	Life Technologies GmbH, Darmstadt, Germany
Bio-Rad	Bio-Rad Laboratories GmbH, Munich, Germany
Biozym	Biozym Scientific GmbH, Hessisch Oldendorf, Germany
Calbiochem, Merck	Merck KGaA, Darmstadt, Germany
Epicentre	Epicentre Biotechnologies, Madison, WI, USA
Eurofins MWG Operon	Eurofins MWG GmbH, Ebersberg, Germany
Fermentas, Thermo Scientific	Thermo Fischer Scientific, Waltham, MA, USA
GE Healthcare	GE Healthcare Deutschland, Munich, Germany
Metabion	Metabion GmbH, Martinsried, Germany
QIAGEN	QIAGEN GmbH, Hilden, Germany
Promega	Promega GmbH, Mannheim, Germany
Carl Roth	Carl Roth GmbH + Co. KG, Karlsruhe, Germany
Serva	SERVA Electrophoresis GmbH, Heidelberg, Germany
Sigma-Aldrich; Sigma Life Science	Sigma-Aldrich Chemie GmbH, Steinheim, Germany

3.1.2 Oligonucleotides

DNA oligonucleotides were designed using the Primer3 software (`http://frodo.wi.mit.edu/primer3/`) and obtained from Sigma Life Science or Eurofins MWG Operon. Sequences of the nucleotides used in this work are provided in the respective methods chapters.

3.1.3 Cyanobacterial strains

The *Synechocystis sp*. PCC 6803 WT strain used for this study was obtained from the culture collection of the Department of Genetics, Humboldt University. It was originally provided by Prof. Sergey V. Shestakov, Chair of Genetics, Lomonossov State University, Moscow. The same strain, but from the culture collection of the Cyanobiotech GmbH, Berlin, was used for experiments with optimized bioreactors.

3.1.4 Escherichia coli strains

Plasmids containing knockout constructs with PCR and resistance cassette inserts were propagated in *E. coli* TOP10 cells (Invitrogen).

3.2 Methods

3.2.1 Cultivation of *Synechocystis* and experimental conditions

3.2.1.1 Cultivation of *Synechocystis*

The cultivation of *Synechocystis* if not otherwise stated was conducted photoautotrophically in BG11 media (Rippka *et al.*, 1979) at 28° C. For handling the strain collection (chapter 2.1.3.) *Synechocystis* cultures were streaked, under sterile conditions, on BG11 solid media with 0. 75 % (w/v) Bacto-Agar (Difco) and incubated under continuous light (white light with intensities of ~50-60 E s^{-1} m^{-2}). For long term conservation aliquots of the generated mutants were transferred into 0.5 x BG11 with 8 % (v/v) DMSO and shock frozen with liquid nitrogen and stored under -80º C. The cultivation of *Synechocystis* in liquid media was done in 20 ml volume in 50 ml Erlenmeyer flask under mild shaking (100 rpm) (if not otherwise statet: light intensity: ~50μE s^{-1} m^{-2}).

3.2.1.2 Experimental conditions

3.2.1.2.1 Optimized photobioreactor

To achieve highly controlled ethanol production conditions, certain experiments have been done in the facilities of Cyanobiofuels GmbH in specialized photo bioreactors, designed to achieve maximum ethanol output per volume of the culture by using a combination of high frequency stirring at 250 rpm and an adaptation of light intensities starting at 100 μE s^{-1} m^{-2}) per unit and followed by a constant increase of light intensities depending on the cell density of the culture. Furthermore, the temperature of the culture was controlled in a day-night cycle with 35° C day-time and 25° C night-time temperature and a computer-based controlled discontinuously aeration of the liquid phase with 10 % CO_2 enriched air during the 12 h photo period to regulate the pH between 7.25 - 7.35 was used. Strains of *Synechocystis* were cultivated in 0.5 L BG11 medium supplemented with 2 mM TES, 35 g l^{-1} "instant

ocean" seawater salts and 10 μg mL^{-1} gentamycin. To avoid nutrition limitation, the nitrate concentration, of the media, was monitored and the cultures were supplemented with 100 x nutrient concentrate in case it reached 50 % of the original concentration. Temperature, pH and dissolved oxygen level were constantly monitored and recorded due the time frame of the experiment. Experiments have been performed in triplicates using *Synechocystis* cultures harboring an empty vector control strain and a mixed distribution of the positions to avoid further side effects.

3.2.1.2.2 Standard laboratory condition

The dilution of the pre-cultures described in (chapter 3.2.1.1.) to a volume of 200 mL and a OD_{750} ~0.8 in specialized 500 mL reactor bottles and a sub sequent adaptation period to the laboratory condition to a optical density OD_{750} of >1.2 was, if not otherwise indicated, the starting point of all experiments conducted under standard laboratory conditions. The caps of the bottles have been prepared with an inflow tube for constant air support with 3 % CO_2 enriched air and an outflow tube with sterile fixed filters. The cultures exhibited constant steering and constant light (light intensity: ~80 μE s^{-1} m^{-2}) at 28° C in a growth chamber. For the selection of mutants antibiotics to the following concentration have been used chloramphenicol (7 μg mL^{-1}), kanamycin (80 μg mL^{-1}) and gentamycin (10 μg mL^{-1}). The supplementations of stress inducing factors are described in the according chapters.

3.2.2 Plasmid isolation

Plasmid isolation was performed as previously described (Sambrook *et al.*, 2001).

3.2.3 Handling of nucleic acids

3.2.3.1 Isolation of nucleic acids from *Synechocystis*

3.2.3.1.1 Isolation of total DNA from Synechocystis

Synechocystis DNA samples where either isolated as described for bacteria (Sambrook *et al.*, 2001) or by boiling of 11 μL of *Synechocystis* cultures with an OD_{750} ~ 1 at 99° C.

3.2.3.1.2 Isolation of total RNA from *Synechocystis*

Total RNA was extracted from previous isolated *Synechocystis* cultures using TRIzol (Invitrogen) following the manufacturer protocol with a "hot Trizol" modification, meaning the boiling of the trizol cultures mixture at 99° C for 5 minutes with frequent vortexing, as the initial step of the isolation. The procedure was conducted the following. First 50 mL sterile falcon test tubes were filled with 25 mL crushed ice. Then an adjusted volume of cell cultures from which the RNA was taken was filled into the test tubes (25 mL at OD_{750} ~ 1, 12.5 mL

at OD_{750} ~2, and so on). The ice mixture was when swiftly centrifuged at 6000 rpm for 15 min and the pellet was resuspended in 1 mL Trizol after this above described "hot Trizol" step was applied. Further the protocol was followed.

3.2.3.2 Determination of nucleic acid concentrations

The DNA and RNA concentration was determined by optical density with a spectrophotometer at 260 nm (Nanodrop; Thermo Scientific) and the integrity of rRNA bands was additionally verified by electrophoresis using 1 % denaturating agarose gels containing 1.7 M formaldehyde. The RNA was stored at -80° C.

3.2.3.3 Purification of the RNA

Materials used for microarray analysis were treated with DNAseI (Ambion) according to the protocol to eliminate remains of DNA in the samples followed by control PCRs.

3.2.3.4 Microarray analyses

10 μg samples of of total RNA were shipped to the microarray conducting company.
Hybridization of the chips and statistical analyses were made by imaGenes GmbH, Germany.

3.2.4 Gel electrophoresis of nucleic acids

Agarose gel electrophoreses of DNA and RNA were performed as previously described (Sambrook *et al.*, 2001).

3.2.5 Polymerase chain reaction (PCR)

PCR reactions were performed using Taq DNA Polymerase (QIAGEN) following the manufacturer's protocol. PCR products were analyzed by agarose gel electrophoresis.

3.2.6 Knockout studies

3.2.6.1 Knockout construction

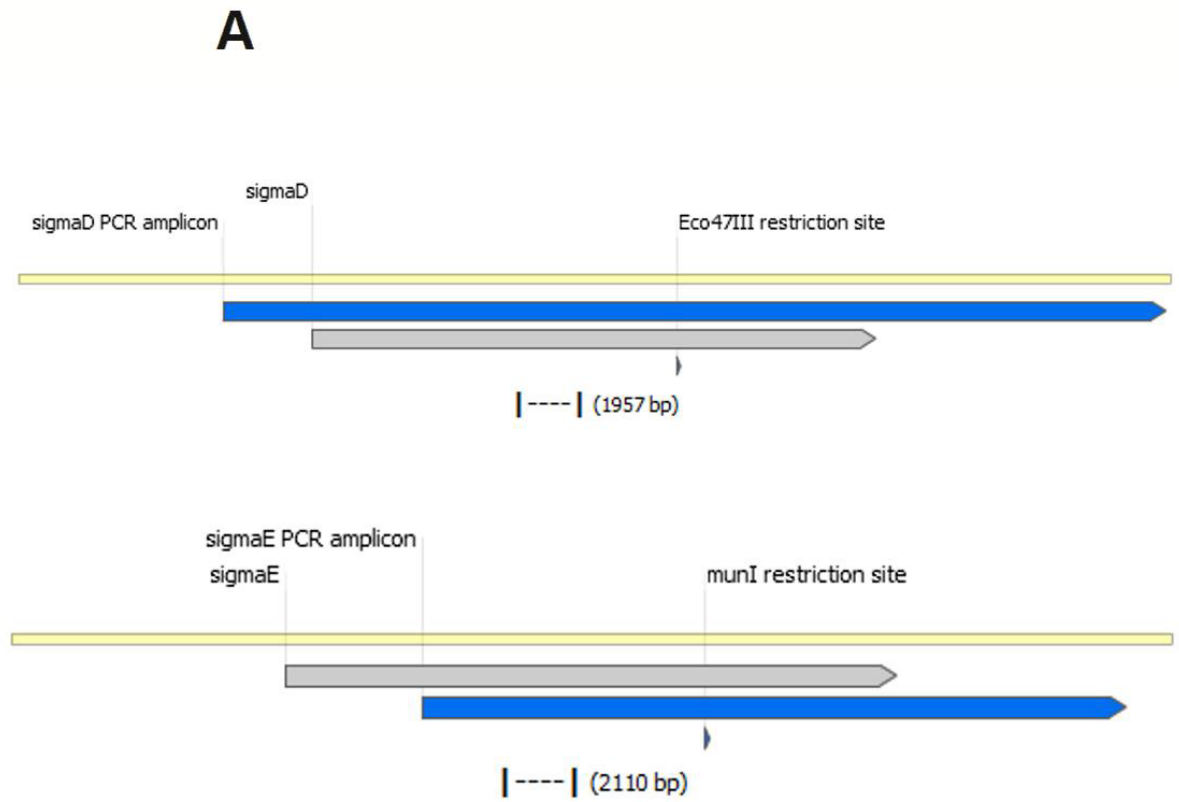

Figure 19: Knockout mutant construction strategy for the *Synechocystis* sigma factors SigD and SigE. The yellow bars mark the genomic region of *sigD* and *sigE* with 1957 bp and 2110 bp, respectively.

The corresponding PCR products of the gene of interest were cloned into a into an open pDrive^{TM} vector (Invitrogen) according to the protocol (Qiagen pDrive Manual). Followed by enzymatic restriction of an according cutting sites (Fig.19) and a reaction with Klenow fragement (Fermentas), according to protocol. The PCR products were religated with a chloramphinicol cassette which originated from a PACYC184 vector cut with BSAa1 (NEB). Constructs have been verified by PCR and sequence analyses with the pDrive multiple cloning site-specific M13 primer.

Gray bars represent the annotated sequences from Cyanobase and blue bars the used PCR amplicons for further cloning. Gray triangles mark the restriction site used for insertion of the antibiotic resistance cassette *Eco47*III and *Mun*I, respectively.

Table 19: List of primers used for sigma D and E knockout studies.

Oligo	***Sequence (5'-3')***
SigD_fw	TCAGTGCTGGGGAGCTATTT
SigD_rv	AATAGGGAGCCAAACGACCT
SigE_fw	AAATTGTCCGCTGTGGTTTC
SigE_rv	TAAAAGGGGCCCTGCTAACT

3.2.6.2 Creating of *Synechocystis* knockout strains

Knock-out constructs have been introduced into *Synechocystis* via natural transformation following a modified transformation protocol previousl described by Zang. *et al.* (2007) without the pretreatment with 2 mM EDTA.

3.2.6.3 Provided knockout strains

Response regulator knockout analyses were used from the Humboldt University collection. The mutant strains were originally kindly provided by Prof. Iwane Suzuki, Japan.

3.2.6.4 Creating ethanologenic *Synechocystis* cultures

Plasmids containing the respective production cassette were transferred into *Synechocystis* via conjugation previousl described (Marraccini *et al.* 1993).

3.2.7 Northern blot analysis

3.2.7.1 Radioactive labeled probes

3.2.7.1.1 RNA Probes

Radioactive labelled RNA probes were made with T7 Maxiscript™ from Ambion applied Biosystems GmbH, according to the manufactures protocol with [α-^{32}P]-UTP from Amersham Bioscience (Freiburg).

3.2.7.1.2 DNA Probes

Radioactive labelled RNA probes were made with DecaLabel™ DNA Labeling Kits (MBI Fermentas) with [α-^{32}P]-dCTP from Amersham Bioscience (Freiburg).

3.2.7.1.3 Oigonucleotides used for Norhern blot studies

Oligonucleotides used for template PCR for the sub sequent use in radioactive labeling reaction can be found in (Tab.20).

Table 20: Oligonucleotides used for Northern blot analysis.

Oligo	***Sequence (5'-3')***
*SigD*ProbeFw	GGTGGTATCTGTCGCCAAAA
*SigD*ProbeT7	TAATACGACTCACTATAGGGCTAGATGTTCCGCCAATTCC
*SigE*Probefw	AAATCCGATTGTTGGTCAGC
*SigE*ProbeT7	TAATACGACTCACTATAGGGCACCAGTAGGCATAGGTGGAA

*SigF*ProbeFw	GCTCCTTTGCCATTCCCTAT
*SigF*ProbeT7	TAATACGACTCACTATAGGGGGCTAAACAATCCCCCAGAT
*SigG*Probefw	GCTTAAACGAACCGGTCAAA
*SigG*ProbeT7	TAATACGACTCACTATAGGGTTCGGCAATTTCTTCGTAGG
*SigH*ProbeFw	TTTTGCCACCTGGCTTTATC
*SigH*ProbeT7	TAATACGACTCACTATAGGGCCGCCGAGCATAGAATAAAC
*SigI*ProbeFw	GGAGACCACCACTCCCTACA
*SigI*ProbeT7	TAATACGACTCACTATAGGGCCAAGGGGAATGGCTAATTT
sll0990ProbeFw	GGGAAGGGGTAACCAGTGTT
sll0990ProbeT7	TAATACGACTCACTATAGGGGGCCATTGTAGGAAAAACGA
slr0942Probefw	TCCAAGCTGTGGAGTAATGC
slr0942ProbeT7	TAATACGACTCACTATAGGGAAGCCGGGGTAAATGGTAGT
slr1192ProbeFw	ATTTAGTGGGGCTGGGTTG
slr1192ProbeT7	TAATACGACTCACTATAGGGAATTTCACCACGCTGACTCC
Sll0449Probefw	ATTGTCAGCGGGTTTCTCTG
Sll0449ProbeT7	TAATACGACTCACTATAGGGTTTCATATTCCGTTCGCACA
*Rre26*ProbeFw	GGTGGTGTTGGATGTGATGA
*Rre26*ProbeT7	TAATACGACTCACTATAGGGAGCGACTCACCAACAATTCC
*cpcG2*ProbeFw	TCCATTGTGATCGCCACTAA
*cpcG2*ProbeT7	TAATACGACTCACTATAGGGGCAACGGCAATTATCCCTAA
*psbA2*Probefw	GCTGGTTCTTTGCTTTACGG
*psbA2*ProbeT7	TAATACGACTCACTATAGGGCACCAAGGAGGAGGTTACCA
*psbM*ProbeFw	GCAAGTTAACAATCTCGGCTTT
*psbM*ProbeT7	TAATACGACTCACTATAGGGATCAACAGGAAAACCGTTGG

*cpcA*_Probe_Fw	CAAACCCAAGGCAACAACTT
*cpcA*_Probe_T7	TAATACGACTCACTATAGGGGCCGTGGTTAGCTTTGATGT
*cpcB*_Probe_Fw	TTGCGTGACATGGAAATCAT
*cpcB*_Probe_Fw	TTGCGTGACATGGAAATCAT
*cpcB*_Probe_T7	TAATACGACTCACTATAGGGCGATTTCAGCAACGATAGCA
*CpcC1*_Probe_Fw	CAAACATCTGTTGGGTCGTG
*CpcC1*_Probe_T7	TAATACGACTCACTATAGGGGATAGGCCCAACCAGCATTA
*CpcC2*_Probe_Fw	GTCAAGTTTTGGGCAACGAT
*CpcC2*_Probe_T7	TAATACGACTCACTATAGGGTTTTTGATTCCGCTGGGTAG
*CpcD*_Probe_Fw	TCTTTGGTGGGCTATTCCAA
*CpcD*_Probe_T7	TAATACGACTCACTATAGGGTGTCAGCTTGATAGGGACGA
*rps8*_fw	CTACTCTGAAACCGGCGAAG
*rps8*_t7	TAATACGACTCACTATAGGGGTGGAAACAATGGCGATACC
sll0588_Probe_Fw	CAGCGCAGATATTTTGGTGA
sll0588_Probe_T7	TAATACGACTCACTATAGGGACGTTGCCGGAGTATCAAAG
slr0284_Probe_Fw	TCGTCTGGATTGTCACCTCA
slr0284_Probe_T7	TAATACGACTCACTATAGGGTGGCGTTGACTACGGTGTAA
sll1191 _Probe_Fw	GAGGGGAGTTTTCGTTGGAT
sll1191 _Probe_T7	TAATACGACTCACTATAGGGTTGTTGTTGGGAAGGGACTC
sll0218 _Probe_Fw	GTTTCCATCGGAGTTGCAGT
sll0218 _Probe_T7	TAATACGACTCACTATAGGGTGATGGGGACTCCTTACCAG
Slr1259_Probe_Fw	GGGGAAATTGTTCATGTTGG
Slr1259_Probe_T7	TAATACGACTCACTATAGGGGTAGTCATGGCCCGGATAGA
Slr1261_Probe_Fw	GCCGACGGTAAAAACAAAAA

Slr1261_Probe_T7	TAATACGACTCACTATAGGGGCCCAAAAGATTAGCCATCA
pilA7 _Probe_Fw	GACTCTCCGACAGGCTCAAC
*pilA7*_Probe_T7	TAATACGACTCACTATAGGGGAATTGCTGTACCGGGAAAA
Slr1770 _Probe_Fw	GGATGGGCTGATTCAAGCTA
Slr1770 _Probe_T7	TAATACGACTCACTATAGGGCAAACTCTTGACGGAGCACA

3.2.7.1.4 Hybridization of the membranes

Blotted nylon membrane were pre hybridized in 11 mL of a mixture of 50 % [v/v] Church buffer (1 % (w/v) bovine serum albumin, 1 mM EDTA, 0.5 M phosphate buffer, 7% (w/v) SDS) and 50 % [v/v] deionized formamide for 1 h at 65° C before they got mixed with the radioactive labelled [α-^{32}P]-UTP RNA or [α-^{32}P]-dCTP DNA probes and incubated for 12 h at 65° C or 55° C respectively. Tubes were carousel mixed at a speed of ~10 rpm in a hybridization oven.

3.2.7.1.5 Finalization / washing of the membranes

Blotted nylon and radioactive labelled membranes were washed with a decreasing concentration of a washing buffer solution with the following concentrations:

2 x SSC / 1 % [w/v] SDS

1 x SSC / 1 % [w/v] SDS

0.5 x SSC / 0.5 % [w/v] SDS

0.5 x SSC / 0.05 % [w/v] SDS

0.05 x SSC / 0.05 % [w/v] SDS

The washing of the membranes were done in plastic boxes in a 65°C for RNA and 55°C for DNA in a heated water bath. Between each washing step a check with a hand held Geiger-Müller counter was performed and in case of a strong decreased signal the washing steps were halted.

3.2.7.1.6 Visualization of the radioactive signals

Radioactive signals were detected and quantified using the molecular Imager FX™ and Quantity One™ software from Bio-Rad GmbH.

3.2.8 Whole-cell absorption spectra of *Synechocystis*

Absorption spectra of *Synechocystis* cultures of whole s in BG11 liquid media with the wave lengths between 400 and 750 nm at room temperature were taken in plastic cuvettes with a spectro photo meter (UV-2410PC, Shimadzu) with a BG11 baseline.

3.2.9 Chlorophyll measurement

The determination of the Chl amount was conducted as previously described by Lichtenthaler (1978). A pellet from 0.5 ml *Synechocystis* cultures was resuspended in 90 % [v/v] methanol and incubated for 1 h at 4° C. After a centrifugation (14000 g for 5 min) the supernatant was spectrometrically measured at a wave length of 665 nm and calculated via the formula Chl [μg ml^{-1}] = OD_{665} nm x 11.5 [μg ml^{-1}] x dilution factor (McMinney, 1941).

3.2.10 Ethanol concentration measurements

Measurements of the ethanol concentrations in experiments with optimized photobioreactors (chapter 2.2.1.2.1.) were performed mass spectrometrically by the technical team of Cyanobiofuels GmbH. Under standard laboratory conditions (chapter 2.2.1.2.2.) a photospectrometrically method with the EnzyChromTM Ethanol Assay Kit (ECET-100) from BioAssay was used to determine the ethanol concentrations. This test is based on an alcohol dehydrogenase catalyzed oxidation of ethanol, in which the formed $NADH^+$ is coupled to a chromogen.

3.2.11 Glycogen and Carotenoid contents determination

Carotenoid content determination via HPLC measurements and determination of the glycogen concentrations were performed by the technical team of Cyanobiofuels GmbH.

3.2.12 Data and graphical visualization

Data visualization was done for graphs with GraphPad™ and tables with Microsoft Excel™. Visualization of genomic regions and genes were performed with j5™ (`http://j5.jbei.org`).

3.2.13 Sequencing

Purified vector DNA was delivered for automatic sequencing to "SMB Service in Molecular Biology" (Berlin). Raw sequence files were viewed and edited with "4Peaks" software (`http://mekentosj.com/4peaks`).

3.2.14 Induction of the ethanol production

The Induction of the ethanol production (if not other stated) was induced by copper depletion. The to inducing culture was centrifugation (4000 g for 5 min) and the resulting cell pallet was resuspended in BG-11 medium without copper.

3.2.15 Blue-native PAGE experiments

Blue-native PAGE experiments were done with pre poured gel chambers from Serva™ according to the manufactures protocol. Protein concentration determination was done as previously described (Sambrook *et al.*, 2001). Thylakoid membrane preparation was done by harvesting cultures, centrifuging them and mixing the pallet at a ratio of 1:3 with thylakoid buffer (50 mM Hepes/NaOH, pH 7.0. 5 mM $MgCl_2$, 25 mM $CaCl_2$, 10 % (v/v) glycerol). Next glass beats with a volume of (0.1-0.5 mm) were mix to the suspension in a ratio of 1:1 and a 10 minute milling with a cell mill (Retsch) at 4° C was applied. The cell were when sedimented by a 2000 RPM centrifugation at 4° C followed by a centrifugation with 14 000 RPM with a resulting thylakoid pallet which was resuspended in 4 volume in thylakoid buffer.

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5 Appendices

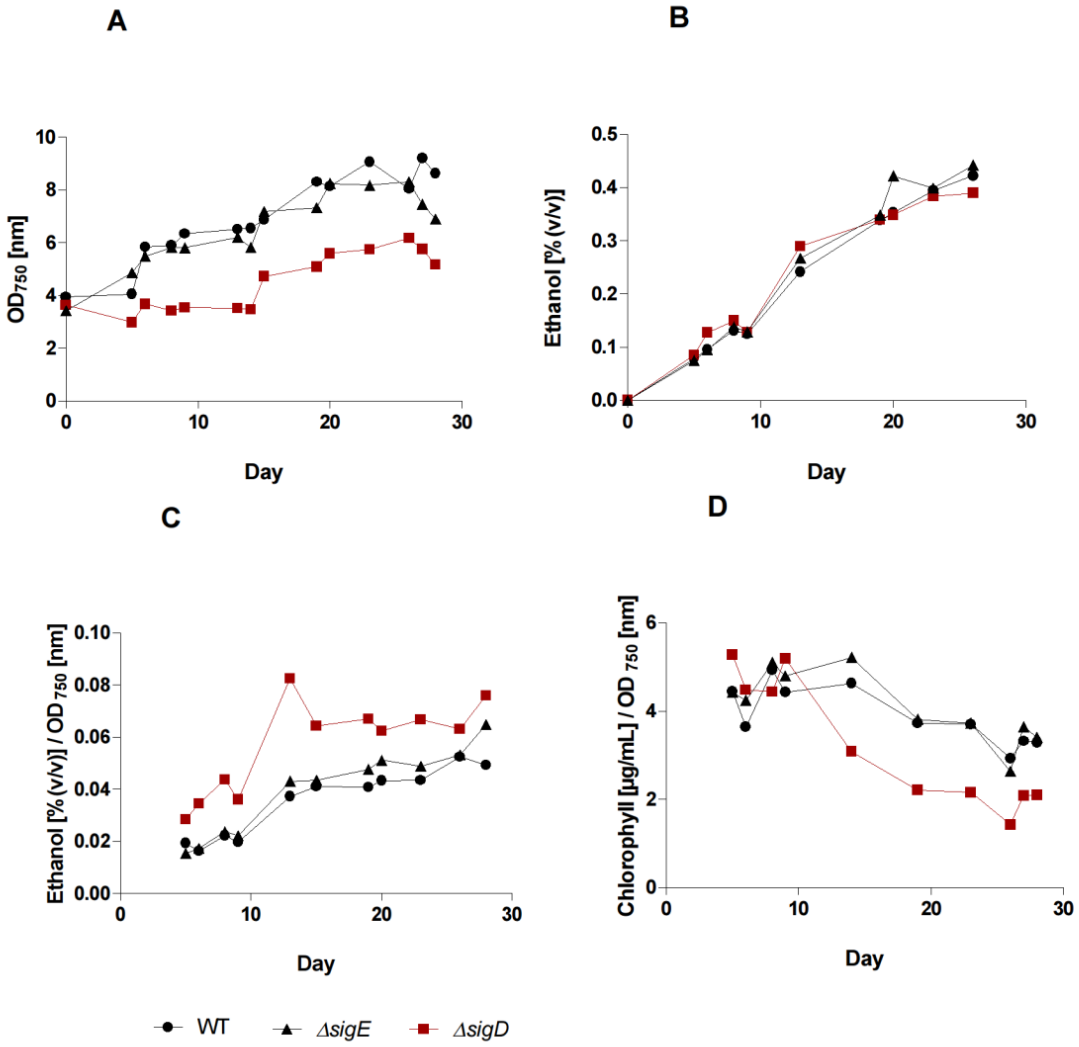
Abbreviations

%	percentage
° C	degree Celsius
ATP	adenosine-5'-triphosphate
ATPase	adenosine triphosphatase
DNA	deoxyribonucleic acid
E.coli	*Escherichia coli*
EDTA	ethylenediaminetetraacetic acid
Kb	kilobase
M	molar
$\mu E\ s^{-1}\ m^{-2}$	micoreinstein per second per square meter
µg	microgram
Min	minute
mL	milliliter
µL	microliter
mM	milimolar
mRNA	messenger RNA
Nm	nanometer
Nt	nucleotide
N	nitrogen
PCR	polymerase chain reaction
PSI	photosystem I
PSII	photosystem II
RNA	ribonucleic acid
RNase	ribonuclease
rpm	round per minute
rRNA	ribosomal RNA
Synechocystis	*Synechocystis sp.* PCC6803
TAE	Tris-acetate EDTA buffer
TCA	tricarboxylic acid
tRNA	transfer RNA
v/v	volume per total volume
w/v	weight per volume
Trx	thioredoxin
Chl	chlorophyll
WT	wild type
Z .moblis	*Zymomonas mobilis*

APPENDIX A: Influencing the regulatory network

In order to analyze, whether the ethanol production capacity of Synechocystis can be elevated by manipulating the global transcriptional machinery, knockout mutants of both previous under acetaldehyde exposure analyzed sigma factors have been constructed. The mutants were conjugated with the ethanologenic construct (chapter 3.2.6.4.) and were analyzed.

The respective ethanologenic *Synechocystis* strains were further analyzed with respect to their ethanol generation as well as to their reproductive ability and their Chl *a* content (supplemental Fig.1).



Supplemental figure 1: Effect of engineered ethanol production on growth, Chl *a* content and ethanol accumulation of sigD and sigE knockout strains of *Synechocystis* compared to the WT. The diagrams A, B, C and D show the optical densities at 750nm (OD_{750}), the

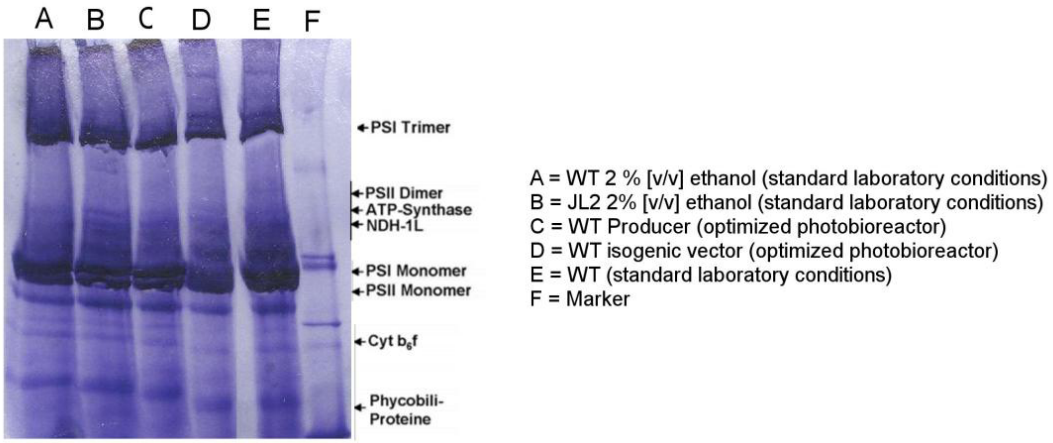
successive ethanol accumulation in the medium, the normalized ethanol concentration per OD_{750} and normalized Chl *a* per OD_{750} content respectively. Squares and triangles mark samples taken from the *sigD* and *sigE* knockouts, respectively. Circles mark samples taken from the ethanologenic control WT strain of *Synechocystis*. Measurements were taken in a time frame of one month.

Ethanologenic ΔSigE strain showed similar growth ethanol accumulationand relative ethanol and Chl *a* content per OD_{750} as the ethanologenic WT strain.

Ethanologenic ΔSigD strain exhibited a greater retardation of growth and relative Chl *a* content, while showing similar amounts of ethanol accumulation, leaving ΔSigD cultures with a seemingly higher ethanol production per cell. Normalization on the net dry weight (Data not shown) indicated a similar picture between the ethanologenic WT and knockout strains and thus challenging the above observation but still giving information on the type of stress ethanol is posing as it is possible that the ΔSigD factor is required for acclimation to conditions that enhance the production of reactive oxygen species (Pollari *et al.*, 2008).

APPENDIX B: Blue-native PAGE analyses of thylakoid membrane complexes

In order to determine if the different phenotypes of JL2 and WT as well as WT with and without the treatment of external ethanol can be seen on protein level of the thylakoid membranes, blue-native PAGE experiments were conducted.



Supplemental figure 2: Analyses of protein complexes of thylakoid membranes with blue-native Page. A, B and E derived from experiments under standard laboratory conditions and C and D from 5 days after the exposure to 2 % [v/v] ethanol on pre-adapted *Synechocystis* JL2 strain (B) compared to the WT with (A) and without (E) ethanol treatment. C and E derived from experiments in optimized photo bioreactors of WT Producer and WT control with an isogenic vector respectively.

Conducted blue-native PAGE experiments of isolated thylakoid membrane complexes show remarkably little difference between JL2 and WT as well as between ethanologenic, non ethanologenic and ethanol treated cells after 5 days (supplemental Fig.4).

APPENDIX C: List of differential regulated genes of ethanol treated and ethanol producing *Synechocystis*

Supplemental Table S1. Overview of changes in gene expression of all 3264 ORF of *Synechocystis* PCC6803 during the exposure to ethanol. The ORF are grouped into functional categories according to Cyanobase. The entries in the Table present the normalized log-intensities, on a 2log-scale, at different time points and different ethanol concentration during the experiment. A yellow-green and orange background indicates ORF that were significantly regulated (Anova: $p<0.05$) at external ethanol or ethanol producer respectively. The table is sorted by functionary groups. Green and blue colors indicate ORF with more than one fold down-regulation and up-regulation, respectively, in their batch-culture experiment. Pale green and pale blue indicate ORF with less than one fold down-regulation and up-regulation, respectively.

ORF	Gene	Product	Cyanobase Cat. number	praw-value	0,05%/0,5h	0,5%/0,5h	0,5%/2h	0,5%/24h	2%/0,5h	Producer
					Normalized log-intensity at different time and concentrations points					
1,1	Amino acid biosynthesis / Aromatic amino acid family									
slr0966	trpA	tryptophan synthase alpha chain	1							
slr0543	trpB	tryptophan synthase beta subunit	1	0,031						0,26
slr0608	hisIE	histidine biosynthesis bifunctional protein HisIE	1							
sll1958	hisC	histidinol phosphate aminotransferase	1							
slr0652	hisA	phosphorybosilformimino-5-amino- phosphorybosil-4-imidazolecarboxamideisomerase	1							
slr0500	hisB	imidazoleglycerol-phosphate dehydratase	1							
slr0682	hisD	histidinol dehydrogenase	1							
slr1848	hisD	histidinol dehydrogenase	1							
sll1893	hisF	cyclase	1							
sll0900	hisG	ATP phosphoribosyltransferase	1							
slr0084	hisH	amidotransferase HisH	1							
slr1867	trpD	anthranilate phosphoribosyltransferase	1							
slr0738	trpE	anthranilate synthetase alpha-subunit	1							
slr0055	trpG	anthranilate synthase component II	1							
sll1112	aroQ	3-dehydroquinate dehydratase	1							
sll0109	aroH	chorismate mutase	1							
slr0444	aroA	3-phosphoshikimate 1-carboxyvinyltransferase	1							
slr2130	aroB	3-dehydroquinate synthase	1							
sll1747	aroC	chorismate synthase	1							
slr1559	aroE	shikimate 5-dehydrogenase	1							
sll1669	aroK	shikimate kinase	1							
slr0546	trpC	indole-3-glycerol phosphate synthase	1	0.006 / 0.031				-0,2	-0,74	
slr1979	trpE	anthranilate synthase component I	1							
sll0356	trpF	N-(5'-phosphoribosyl)anthranilate isomerase	1							
slr2081	tyrA	prephenate dehydrogenase	1							
sll1662		probable prephenate dehydratase	1							
sll1713	hisC	histidinol-phosphate aminotransferase	1							
sll0084		putative phosphatase	1							
1,2	Amino acid biosynthesis / Aspartate family		1							
sll0402	aspC	aspartate aminotransferase	1							
sll0455	thrA	homoserine dehydrogenase	1							
sll1172	thrC	threonine synthase	1							
slr0549	asd	aspartate beta-semialdehyde dehydrogenese	1	0,024					0,48	
sll1688	thrC	threonine synthase	1	0,004					1,23	
sll1760	thrB	homoserine kinase	1	0,007						1,03
slr0212	metH	5-methyltetrahydrofolate--homocysteine methyltransferase	1							
sll1444		3-isopropylmalate dehydratase small subunit	1							
sll1058	dapB	dihydrodipicolinate reductase	1	0,040						
slr1665	dapF	diaminopimelate epimerase	1							
sll0006		putative aminotransferase	1							
slr0036	aspC	aspartate aminotransferase	1							
1,3	Amino acid biosynthesis / Branched chain family		1							
slr2072	ilvA	L-threonine deaminase	1	0,002						1,14
sll1363	ilvC	ketol-acid reductoisomerase	1	0,006			-0,24			
slr0452	ilvD	dihydroxyacid dehydratase	1	0,040						0,65
slr2088	ilvG	acetohydroxy acid synthase	1							
slr1517	leuB	3-isopropylmalate dehydrogenase	1							
slr0550	dapA	dihydrodipicolinate synthase	1							
sll0065	ilvN	acetolactate synthase small subunit	1							
sll0504	lysA	diaminopimelate decarboxylase	1							
slr0032		probable branched-chain amino acid aminotransferase	1							
slr0186	leuA	2-isopropylmalate synthase	1							
sll1470	leuC	3-isopropylmalate dehydratase large subunit	1							
sll1564		putative lyase	1							

sll1981	ilvB	acetolactate synthase	1	0,007						-0,42
1,4	Amino acid biosynthesis / Glutamate family / Nitrogen assimilatic		1							
slr0710	gdhA	glutamate dehydrogenase (NADP+)	1	0,033						0,61
sll1499	glsF	ferredoxin-dependent glutamate synthase	1							
sll0704	nifS	cysteine desulfurase	1							
sll0601		nitrilase homolog	1							
sll0373	proA	gamma-glutamyl phosphate reductase	1							
sll1454	narB	ferredoxin-nitrate reductase	1							
sll0080	argC	N-acetyl-gamma-glutamyl-phosphate reductase	1							
slr0585	argG	argininosuccinate synthetase	1							
slr0288	glnN	glutamate--ammonia ligase	1							
slr0898	nirA	ferredoxin--nitrite reductase	1							
slr1022	argD	N-acetylornithine aminotransferase	1							
ssl0707	glnB	nitrogen regulatory protein P-II	1							
slr0899	cynS	cyanate lyase	1	0,030				-0,56		
sll0902	argF	ornithine carbamoyltransferase	1							
sll0100		N-acyl-L-amino acid amidohydrolase	1							
slr1133	argH	L-argininosuccinate lyase	1							
sll1883	argJ	arginine biosynthesis bifunctional protein ArgJ	1							
ssl2667	cnfU, synif	an assembly factor for iron-sulfur culsters	1							
slr1898	argB	N-acetylglutamate kinase	1							
slr1756	glnA	glutamate--ammonia ligase	1							
sll1502	gltB	NADH-dependent glutamate synthase large subunit	1	0,010	0,52					
sll1027	gltD	NADH-dependent glutamate synthase small subunit	1							
sll0784	merR	nitrilase	1							
slr0387	nifS	cysteine desulfurase NifS	1							
slr0077	nifS	cysteine desulfurase	1	0,017						-0,7
sll0450	norB	cytochrome b subunit of nitric oxide reductase	1							
slr0395	ntcB	nitrate assimilation transcriptional activator, LysR family protein	1							
sll0461	proA	gamma-glutamyl phosphate reductase	1							
slr2035	proB	glutamate 5-kinase	1							
slr0661	proC	pyrroline-5-carboxylate reductase	1							
slr2143		L-cysteine/cystine lyase	1							
slr1653		N-acyl-L-amino acid amidohydrolase	1							
slr1529		nitrogen assimilation regulatory protein	1							
slr0644		nitrogen regulation protein NifR3 homolog	1	0,003		0,17				
slr2079		putative glutaminase	1	0,015						0,44
1,5	Aminoacid biosynthesis / Serine family / Sulfur assimilation		1							
slr1842	cysK	cysteine synthase	1							
sll1931	glyA	serine hydroxymethyltransferase	1	0,026					-0,37	
slr1165		sulfate adenylyltransferase	1							
slr1791	cysH	phosphoadenosine phosphosulfate reductase	1							
slr0963	sir	ferredoxin-sulfite reductase	1							
slr0676	cysC	adenylylsulfate kinase	1	0,042					-1,28	
slr1348	cysE	serine acetyltransferase	1							
sll0712	cysM	cysteine synthase	1							
sll1908	serA	D-3-phosphoglycerate dehydrogenase	1	0,021					-0,37	
2,1	Biosynthesis of cofactors, prosthetic groups, and carriers / Biotin		2							
slr1364	bioB	biotin synthetase	2	0,030						0,4
slr0917	bioF	7-keto-8-aminopelargonic acid synthetase	2							
slr0523		similar to dethiobiotin synthetase	2	0,023						-0,3
2,2	Biosynthesis of cofactors, prosthetic groups, and carriers / Carote		2							
slr0739	crtE	geranylgeranyl pyrophosphate synthase	2							
slr0940	crtQ-2	zeta-carotene desaturase	2							
slr1254	pds, crtD,	phytoene dehydrogenase (phytoene desaturase)	2							
sll0254		probable phytoene dehydrogenase Rieske iron-sulfur component	2							
slr0088	crtO	beta-carotene ketolase	2	0,027						0,49
sll1468	crtR	beta-carotene hydroxylase	2							
slr1255	pys, crtB	phytoene synthase	2	0,014				0,53		
slr1125		probable glucosyl transferase	2							
slr1293		similar to to phytoene dehydrogenase	2	0,029						0,41
2,3	Biosynthesis of cofactors, prosthetic groups, and carriers / Cobal		2							
slr0772	chlB	light-independent protochlorophyllide reductase subunit ChlB	2							
slr1030	chlI	magnesium protoporphyrin IX chelatase subunit I	2							
slr0749	chlL	light-independent protochlorophyllide reductase iron protein subunit ChlL	2							
sll1091	chlP	geranylgeranyl hydrogenase	2							
sll1994	hemB	porphobilinogen synthase (5-aminolevulinate dehydratase)	2							
slr0536	hemE	uroporphyrinogen decarboxylase	2							
sll0017	hemL	glutamate-1-semialdehyde aminomutase	2							
sll1184	ho1	heme oxygenase	2							
slr0506	por	light-dependent NADPH-protochlorophyllide oxidoreductase	2							
slr1238	gshB	glutathione synthetase	2							-0,41
slr1055	chlH	magnesium protoporphyrin IX chelatase subunit H	2							

sll1185	hemF	coproporphyrinogen III oxidase, aerobic (oxygen-dependent)	2	0,018		-0,49				
slr1467		precorrin isomerase	2							
sll0378	cobA	uroporphyrin-III C-methyltransferase	2							
slr0969	cobJ	precorrin methylase	2							
slr1368	cobL	precorrin decarbocylase	2							
slr0618	cobQ	cobyric acid synthase	2							
sll1685	pxcA, cotA	protein involved in light-induced Na+-dependent proton extrusion	2							
sll1890		cobalt-chelatase subunit CobN-like protein	2							
slr1887	hemC	porphobilinogen deaminase (hydroxymethylbilane synthase, preuroporphyrinogen synthase)	2	0,044						0,23
sll1876	hemN	coproporphyrinogen III oxidase, anaerobic (oxygen-independent)	2	0,002					-0,61	
sll1875	ho2	heme oxygenase	2							
slr0905	bchE	Mg-protoporphyrin IX monomethyl ester oxidative cyclase	2							
slr1784	bvdR	biliverdin reductase	2	0,002		-0,48				
slr1777	chlD	magnesium protoporphyrin IX chelatase subunit D	2	0,038						0,33
slr0056	chlG	chlorophyll a synthase	2	0,013	0,63					
slr0525	chlM	Mg-protoporphyrin IX methyl transferase	2	0,034						0,48
sll0166	cobA/hemL	a fusion protein between uroporphyrinogen-III C-methyltransferase (CobA/CorA) and uroporphyrinogen-III synthase (HemD)	2							
sll1501	cobB	cobyrinic acid a,c-diamide synthase	2							
slr1925	cobD	cobalamin biosynthesis protein CobD	2							
sll0916	cobH	precorrin isomerase, precorrin-8X methylmutase	2							
slr1879	cobI	precorrin-2 methyltransferase	2							
sll0099	cbiE, cbiT,	precorrin-6y C5, 15-methyltransferase (decarboxylating)	2	0,028				-0,96		
slr0239	cobM	precorrin-4 C11-methyltransferase	2	0,015						-0,54
slr1211	cobN	cobalt-chelatase subunit CobN	2							
slr0260	cobO	cob(I)alamin adenosyltransferase	2							
slr0216	cobP	bifunctional cobalamin biosynthesis protein CobP	2							
slr0502	cobW	cobalamin synthesis protein cobW homolog	2	0,048				-0,96		
sll0794	corR, coaR	cobalt-dependent transcriptional regulator	2							
slr0839	hemH, scp	ferrochelatase	2							
sll1237	hemK	N(5)-glutamine methyltransferase	2							
sll1917	hemN	coproporphyrinogen III oxidase, anaerobic (oxygen-independent)	2							
slr1538		cobalamin biosynthesis protein D	2							
sll0383		cobalamin biosynthesis protein M	2	0,029						-1,62
slr0636		probable cobalamin [5'-phosphate] synthase	2							
slr1742		probable cobyric acid synthase	2	0,013						0,59
slr0252		probable precorrin-6x reductase	2							
2,4	Biosynthesis of cofactors, prosthetic groups, and carriers / Folic A		2							
slr0426	folE	GTP cyclohydrolase I	2							
slr1093	folK	2-amino-4-hydroxy-6-hydroxymethyldihydropteridine pyrophosphokinase	2							
slr2026	folP	dihydropteroate synthase	2							
sll0753	folD	FolD bifunctional protein	2							
sll1612	folC	folylpolyglutamate synthase	2							
slr0994		lipoate-protein ligase B	2							
sll0868		lipoic acid synthetase	2							
slr1598		lipoic acid synthetase	2							
2,5	Biosynthesis of cofactors, prosthetic groups, and carriers / Menac		2							
sll1127	menB	1,4-dihydroxy-2-naphthoate synthase	2							
slr1300		similar to 2-octaprenyl-6-methoxyphenol hydroxylase	2							
slr1518	menA	phylloquinone biosynthesis protein, probable 1,4-dihydroxy-2-naphthoic acid phytyltransferase	2	0,047				0,45		
sll0603	menD	menaquinone biosynthesis protein MenD	2	0,036		0,37				
slr0492	menE	O-succinylbenzoic acid-CoA ligase	2							
slr0611	sds	solanesyl diphosphate synthase	2							
slr0926	ubiA	4-hydroxybenzoate-octaprenyl transferase	2							
slr1099	ubiX	3-octaprenyl-4-hydroxybenzoate carboxy-lyase	2	0,046						0,49
sll0409		similar to O-succinylbenzoate-CoA synthase	2							
2,6	Biosynthesis of cofactors, prosthetic groups, and carriers / Molyb		2							
slr0900	moeA	molybdopterin biosynthesis MoeA protein	2							
slr0901	moaA	molybdopterin biosynthesis protein A	2							
ssr1527		probable molybdopterin [MPT] converting factor, subunit 1	2	0,004		0,84				
slr0902	moaC	molybdenum cofactor biosynthesis protein C, fused to molybdopterin-guanine dinucleotide biosynthesis protein MobA	2							
slr0903	moaE	molybdopterin (MPT) converting factor, subunit 2	2							
sll1536	moeB	molybdopterin biosynthesis MoeB protein	2	0,042						-0,51
2,7	Biosynthesis of cofactors, prosthetic groups, and carriers / Nicoti		2							
slr1239	pntA	pyridine nucleotide transhydrogenase alpha subunit	2	0,049				-0,7		
slr1434	pntB	pyridine nucleotide transhydrogenase beta subunit	2							

slr0936	nadC	nicotinate-nucleotide pyrophosphorylase	2							
slr1691		glutamine-dependent NAD(+) synthetase	2	0,020						0,45
2,8	Biosynthesis of cofactors, prosthetic groups, and carriers / Others		2							
ssl2296		pterin-4a-carbinolamine dehydratase	2	0,036						-0,52
slr1706		dihydroflavonol 4-reductase	2							
2,9	Biosynthesis of cofactors, prosthetic groups, and carriers / Panth		2							
sll0892	panD	aspartate 1-decarboxylase	2							
slr0526	panB	3-methyl-2-oxobutanoate hydroxymethyltransferase	2	0,044				0,48		
sll1249	panC	pantothenate synthetase/cytidylate kinase	2							
sll0250		pantothenate metabolism flavoprotein	2							
2,1	Biosynthesis of cofactors, prosthetic groups, and carriers / Pyrido		2							
slr1779	pdxJ	pyridoxal phosphate biosynthetic protein PdxJ	2							
sll1440	pdxH	pyridoxamine 5'-phosphate oxidase	2							
sll0660	pdxA	pyridoxal phosphate biosynthetic protein PdxA	2							
2,11	Biosynthesis of cofactors, prosthetic groups, and carriers / Quino		2							
sll0631	nadB	L-aspartate oxidase	2	0,041						0,27
sll0622	nadA	quinolinate synthetase	2							
2,12	Biosynthesis of cofactors, prosthetic groups, and carriers / Ribofl		2							
sll1282	ribH	riboflavin synthase beta subunit	2							
slr0066	ribD	riboflavin biosynthesis protein RibD	2							
sll1894	ribA	riboflavin biosynthesis protein RibA	2							
sll0300	ribC	riboflavin synthase alpha chain	2							
slr1882	ribF	riboflavin biosynthesis protein RibF	2							
2,13	Biosynthesis of cofactors, prosthetic groups, and carriers / Thiam		2							
slr0118	thiC	thiamine biosynthesis protein ThiC	2							
sll0635	thiE	probable thiamine-phosphate pyrophosphorylase	2							
slr0633	thiG	thiamine biosynthesis protein ThiG	2	0,044					-1,17	
slr1787		thiamine-monophosphate kinase	2							
2,14	Biosynthesis of cofactors, prosthetic groups, and carriers / Thiore		2							
sll1147		glutathione S-transferase	2	0,010				0,87		
slr0750	chlN	light-independent protochlorophyllide reductase subunit ChlN	2							
sll0554	ftrC	ferredoxin-thioredoxin reductase, catalytic chain	2	0,037				1,19		
slr0623	trxA	thioredoxin	2	0,002				0,93		
slr1139	trxA	thioredoxin	2							
slr0236		similar to glutathione S-transferase	2							
slr1171	gpx1	glutathione peroxidase-like NADPH peroxidase,glutathione peroxidase	2	0.045 / 0.040						-0,53
ssr2061		glutaredoxin	2	0,043						0,68
sll0067		glutathione S-transferase	2							
slr1992	gpx2	glutathione peroxidase-like NADPH peroxidase	2							
sll1545		glutathione S-transferase	2							
slr0233	trxM1	thioredoxin M	2							
sll1057	trxM2	thioredoxin M	2							
slr1846	ycf64	hypothetical protein YCF64	2							
slr0600		NADP-thioredoxin reductase	2							
ssr0330	ftrV	ferredoxin-thioredoxin reductase, variable chain	2							
slr1269	ggt	gamma-glutamyltranspeptidase	2	0,017						0,32
slr1562		glutaredoxin	2							
3,1	Cell envelope / Membranes, lipoproteins, and porins		3							
sll1187		prolipoprotein diacylglyceryl transferase	3							
sll1271		probable porin; major outer membrane protein	3							
sll1550		probable porin; major outer membrane protein	3							
slr1908		probable porin; major outer membrane protein	3							
slr1272		probable porin; major outer membrane protein	3							
slr1841		probable porin; major outer membrane protein	3	0,012				0,85		
slr0993		putative peptidase	3							
slr0819		apolipoprotein N-acyltransferase	3							
slr1227		chloroplastic outer envelope membrane protein homolog	3	0,029						0,45
slr0495		HetI protein homolog	3	0,042					0,81	
sll0772		probable porin; major outer membrane protein	3							
slr0042		probable porin; major outer membrane protein	3							
3,2	Cell envelope / Murein sacculus and peptidoglycan		3							
sll0657		phospho-N-acetylmuramoyl-pentapeptide-transferase	3							
slr0624		UDP-N-acetylglucosamine 2-epimerase	3	0,041				0,76		
slr0804		probable D-alanyl-D-alanine carboxypeptidase	3	0,022	0,77					
slr0534		probable transglycosylase	3							
slr0827		alanine racemase	3							
slr1746		glutamate racemase	3							
slr0646		probable D-alanyl-D-alanine carboxypeptidase	3							
slr0017	murA	UDP-N-acetylglucosamine 1-carboxyvinyltransferase	3							
slr1924		D-alanyl-D-alanine carboxypeptidase, periplasmic protein	3							
slr1423	murC	UDP-N-acetylmuramate-alanine ligase	3							
sll2010	murD	UDP-N-acetylmuramoylalanine--D-glutamate ligase	3							
slr0528	murE	UDP-N-acetylmuramoylalanyl-D-glutamate--2, 6-diaminopimelate ligase	3	0,008				0,94		

slr1351	murF	UDP-N-acetylmuramoylalanyl-D-glutamyl-2 6-diaminopimelate--D-alanyl-D-alanine ligase	3							
slr1656	murG	UDP-N-acetylglucosamine--N-acetylmuramyl-(pentapeptide) pyrophosphoryl -undecaprenol N-acetylglucosamine transferase	3							
slr0191		amidase enhancer, periplasmic protein	3							
slr1874		D-alanine--D-alanine ligase	3							
slr0891		N-acetylmuramoyl-L-alanine amidase	3							
slr1744		N-acetylmuramoyl-L-alanine amidase, periplasmic protein	3							
sll0016		probable membrane-bound lytic transglycosylase A	3							
slr1910		probable N-acetylmuramoyl-L-alanine amidase	3							
slr1708		probable peptidase	3							
slr0938		probable UDP-N-acetylmuramyl tripeptide synthetase	3							
sll0828		putative amidase	3							
sll0899		UDP-N-acetylglucosamine pyrophosphorylase	3							
3,3	Cell envelope / Surface polysaccharides, lipopolysaccharides and		3							
sll1213		GDP-fucose synthetase	3	0,005						0,5
sll0379		acyl-[acyl-carrier-protein]--UDP-N-acetylglucosamine o-acyltransferase	3							
sll0207	rfbA	glucose-1-phosphate thymidylyltransferase	3	0,032				-0,94		
slr1615	rfbE	perosamine synthetase	3							
slr1064		plobable glycosyltransferase	3	0,039						
slr1933	rfbC	dTDP-4-dehydrorhamnose 3,5-epimerase	3							
sll0083		phosphoheptose isomerase	3							
sll1568		fibrillin	3	0,030				0,26		
slr1072		GDP-D-mannose dehydratase	3	0,010						-0,91
slr2116		probable glycosyltransferase	3							
slr0344		probable glycosyltransferase	3							
slr0985	rfbC	dTDP-4-dehydrorhamnose 3,5-epimerase	3	0,014						
slr0983	rfbF	glucose-1-phosphate cytidylyltransferase	3							
slr0984	rfbG	CDP-glucose 4,6-dehydratase	3							
slr2114		perosamine synthetase	3							
sll1535		putative sugar transferase	3							
slr0809	rfbB	dTDP-glucose 4,6-dehydratase	3							
slr0836	rfbB	dTDP-glucose 4,6-dehydratase	3							
sll1395	rfbD	dTDP-6-deoxy-L-mannose-dehydrogenase	3							
slr1024		fibrillin	3							
slr0015		lipid A disaccharide synthase	3							
slr0847		phosphopantetheine adenylyltransferase	3							
slr1962		probable extracellular solute-binding protein	3	0,002					-0,7	
sll1457		probable glycosyltransferase	3							
sll1724		probable glycosyltransferase	3							
sll0380		probable glycosyltransferase	3							
slr1271		probable UDP-N-acetyl-D-mannosaminuronic acid transferase	3							
slr1118		probable UDP-N-acetyl-D-mannosaminuronic acid transferase	3							
3,4	Cell envelope / Surface structures		3							
slr0583		similar to GDP-fucose synthetase	3	0,030						0,4
sll1508		UDP-3-0-acyl N-acetylglcosamine deacetylase	3	0,018					0,5	
slr1424		UDP-N-acetylenolpyruvoylglucosamine reductase	3	0,017				0,22		
4,1	Cellular processes / Cell division		4							
sll1633	ftsZ	cell division protein FtsZ	4	0.007456776 / 0.00936114				-0,4	-0,54	
sll1463	ftsH	cell division protein FtsH	4	0,014				-1,06		
slr1747		cell death suppressor protein Lls1 homolog	4							
sll0169		cell division protein Ftn2 homolog	4							
slr1604	ftsH	cell division protein FtsH	4	0,019				-0,7		
slr1267	ftsW	cell division protein FtsW	4	0,032						1,01
slr0228	ftsH	cell division protein FtsH	4							
slr1390	ftsH	cell division protein FtsH	4	0,043	-0,31					
slr2102	ftsY	cell division protein FtsY	4							
slr0072	gidB	glucose inhibited division protein B	4							
sll0288	minC	septum site-determining protein MinC	4							
sll0289	minD	septum site-determining protein MinD	4							
ssl0546	minE	septum site-determining protein MinE	4							
sll0204		glucose inhibited division protein	4							
4,2	Cellular processes / Cell killing		4							
sll1384		similar to DnaJ protein	4							
sll0202		glucose inhibited division protein	4	0,002				-0,99		
slr0950		hemolysin-like protein	4	0,010				-0,8		
sll0720		RTX toxin activating protein homolog	4	0,037	0,8					
4,3	Cellular processes / Chaperones		4							
sll0058	dnaK1	DnaK protein 1, heat shock protein 70, molecular chaperone	4	0,012				-0,56		
sll1514	hspA	16.6 kDa small heat shock protein, molecular chaperone	4	0,034						0,49
sll0170	dnaK2	DnaK protein 2, heat shock protein 70, molecular chaperone	4							

sll0430	htpG	HtpG, heat shock protein 90, molecular chaperone	4	0,012						-1,12
sll1666		DnaJ-like protein	4							
sll1932	dnaK	DnaK protein	4							
sll0416	groEL-2	60 kDa chaperonin 2, GroEL2, molecular chaperone	4							
slr0093	dnaJ	DnaJ protein, heat shock protein 40, molecular chaperone	4	0,041						0,7
sll0897	dnaJ	DnaJ protein, heat shock protein 40, molecular chaperone	4							
sll1933	dnaJ	DnaJ protein, heat shock protein 40, molecular chaperone	4							
slr2076	groEL1	60kD chaperonin	4	0.02 / 0.019			0,25			-1,55
slr2075	groES	10kD chaperonin	4							
sll0057	grpE	heat shock protein GrpE	4	0,024						
sll1988	hsp33	33 kDa chaperonin	4	0,011					-0,42	
slr0086		similar to DnaK protein	4							
sll1181		similar to hemolysin secretion protein	4							
4,3	Cellular processes / Chemotaxis		4							
slr0162	pilC	a part of pilC, pilin biogenesis protein, required for twitching motility	4							
slr0161	pilT1	twitching motility protein PilT	4							
slr1274	pilM	probable fimbrial assembly protein PilM, required for motility	4	0,024					0,29	
sll1533	pilT2	twitching mobility protein	4							
sll0041	pixJ1, pisJ	phytochrome-like photoreceptor protein for positive phototaxis; homologous to methyl-accepting chemotaxis protein	4							
sll0042	pixJ2, pisJ	methyl-accepting chemotaxis protein for positive phototaxis	4	0,018				-0,43		
sll1694	pilA1	pilin polypeptide PilA1	4	0,009						
slr1043	cheW	similar to chemotaxis protein CheW	4	0,025				0,59		
slr1929	pilA6	type 4 pilin-like protein	4							
sll1294		methyl-accepting chemotaxis protein	4							
slr1044	ctr1	methyl-accepting chemotaxis protein, required for the biogenesis of thick pilli	4	0,036	0,48					
sll1695	pilA2	pilin polypeptide PilA2	4							
slr0163	pilC'	a part of pilC, pilin biogenesis protein, required for twitching motility	4							
sll0040	pixI, pisI	positive phototaxis protein, homologous to chemotaxis protein CheW	4							
slr1120		type 4 prepilin-like proteins leader peptide processing enzyme	4							
sll1107		type IV pilus biogenesis protein PilI homolog	4							
4,4	Cellular processes / Detoxification		4							
sll1987	cpx, katG	catalase peroxidase	4							
ssr2784		antitoxin ChpI homolog	4							
slr1516	sodB	superoxide dismutase	4							
sll0755	tpx, ycf42	thioredoxin peroxidase	4	0,006				-1,02		
sll1980	trxA	thiol:disulfide interchange protein TrxA	4							
sll1615		thiophen and furan oxidation protein	4							
4,5	Cellular processes / Protein and peptide secretion		4							
slr0774	secD	protein-export membrane protein SecD	4	0,022						0,6
sll1814	secY	preprotein translocase SecY subunit	4							
sll0716		leader peptidase I (signal peptidase I)	4	0,034				-0,73		
sll0533		trigger factor	4							
ssl3335	secE	preprotein translocase SecE subunit	4							
slr1277		pilus assembly protein homologous to general secretion pathway protein D	4							
slr1377		leader peptidase I (signal peptidase I)	4							
ssr3307	secG, ycf4	preprotein translocase SecG subunit	4							
sll0194	ycf43	putative sec-independent protein translocase	4							
slr1366		lipoprotein signal peptidase (signal peptidase II)	4							
slr1531	ffh	signal recognition particle protein	4							
slr0063	pilB1	pilus biogenesis protein homologous to general secretion pathway protein E	4							
sll0616	secA	preprotein translocase SecA subunit	4	0,028						0,13
slr0775	secF	protein-export membrane protein SecF	4							
slr0079		probable general secretion pathway protein E	4							
4,6	Cellular processes / Transformation		4							
ssl2923	vapC	similar to virulence-associated protein VapC	4							
sll1929	comE	competence protein ComE	4							
slr0904	comM	competence protein ComM homolog	4							
ssl2922	vapB	similar to virulence-associated protein VapB	4							
slr0427		putative competence-damage protein	4							
sml0009		similar to virulence-associated protein VapC	4							
slr0488		virulence factor MviN homolog.	4	0,009						
5,1	Central intermediary metabolism / amino sugars		5							
sll0220	glmS	L-glutamine:D-fructose-6-P amidotransferase	5							
5,2	Central intermediary metabolism / other		5							
sll1639	ureD	urease accessory protein D	5							
slr1899	ureF	urease accessory protein F	5							

sll1750	ureC	urease alpha subunit	5							
sll0643	ureG	urease accessory protein G	5							
slr1256	ureA	urease gamma subunit	5							
sll0420	ureB	urease beta subunit	5	0,049						-0,55
slr1219	ureE	urease accessory protein E	5	0,029						0,6
5,2	Central intermediary metabolism / phosporous compounds		5							
slr1622	ppa	soluble inorganic pyrophosphatase	5							
sll1676		4-alpha-glucanotransferase	5							
sll1546	ppx	exopolyphosphatase	5	0,033						
5,3	Central intermediary metabolism / Polysaccharides and glycoprot		5							
sll0945	glgA	glycogen synthase	5							
sll1393	glgA	glycogen (starch) synthase	5	0,006				-1,09		
slr1176		glucose-1-phosphate adenylyltransferase	5							
slr1857		isoamylase	5							
sll0290	ppk	polyphosphate kinase	5	0,014						
slr1830	phaC	poly(3-hydroxyalkanoate) synthase	5							
slr0518		similar to alpha-L-arabinofuranosidase B	5							
sll1540		dolichyl-phosphate-mannose synthase	5							
slr1367		glycogen phosphorylase	5							
slr1334		phosphoglucomutase/phosphomannomutase	5							
slr0237		glycogen operon protein GlgX homolog	5							
slr0897		probable endoglucanase	5							
sll1566	ggpS	glucosylglycerolphosphate synthase	5							
sll0158	glgB	1,4-alpha-glucan branching enzyme	5							
sll1356		glycogen phosphorylase	5							
sll0842		neopullulanase	5	0,012				-1,8		
sll0726		phosphoglucomutase	5							
slr1943		probable glycosyltransferase	5	0.039 / 0.042		0,23				-0,46
slr0820		probable glycosyltransferase	5							
slr0323		putative alpha-mannosidase	5							
6,1	Energy metabolism / Amino acids and amines		6							
sll0422		asparaginase	6							
sll0107		KHG/KDPG aldolase	6							
sll0329		6-phosphogluconate dehydrogenase	6							
slr0662		arginine decarboxylase	6							
sll1641		glutamate decarboxylase	6							
sll0370	pyrA	carbamoyl-phosphate synthase, pyrimidine-specific, large chain	6							
sll1077	speB2	agmatinase	6	0,043						0,72
slr1705		aspartoacylase	6							
sll0573		carbamate kinase	6	0,019					0,81	
sll1561	putA	proline oxidase	6							
sll0228	speB1	arginase	6							
slr1877		2-hydroxyhepta-2,4-diene-1,7-dioate isomerase	6							
slr0229		3-hydroxyisobutyrate dehydrogenase	6							
sll1234		adenosylhomocysteinase	6							
sll1682		alanine dehydrogenase	6							
slr1312		arginine decarboxylase	6							
slr0657		aspartate kinase	6							
sll0938		aspartate transaminase	6							
slr0879		glycine decarboxylase complex H-protein	6							
slr0293		glycine dehydrogenase	6	0,029					-1,26	0,62
sll1683		lysine decarboxylase	6							
slr0090		probable 4-hydroxyphenylpyruvate dioxygenase	6	0,038						-0,37
sll0171		probable aminomethyltransferase	6							
sll1178		probable carbamoyl transferase	6							
slr0370		succinate-semialdehyde dehydrogenase (NADP+)	6							
6,1	Energy metabolism / Glycolate pathway		6							
sll1189	glcE	glycolate oxidase subunit GlcE	6							
sll1349		phosphoglycolate phosphatase	6							
sll0404	glcD	glycolate oxidase subunit GlcD	6							
sll1831		glycolate oxidase subunit, (Fe-S)protein	6							
6,2	Energy metabolism / Glycolysis		6							
slr0394	pgk	phosphoglycerate kinase	6							
slr0752		enolase	6	0,014					-1,04	
slr1124		phosphoglycerate mutase	6							
sll0018	fbaA, fda	fructose-bisphosphate aldolase, class II	6							
slr1843	zwf	glucose 6-phosphate dehydrogenase	6							
sll1498		carbamoyl-phosphate synthase small chain	6							
slr1349		glucose-6-phosphate isomerase	6							
sll1196		phosphofructokinase	6							
slr0952	fbpII	fructose-1,6-bisphosphatase	6							
slr0943	fda	fructose-bisphosphate aldolase, class I	6							
slr1945		2,3-bisphosphoglycerate-independent phosphoglycerate mutase	6	0,036				-0,92		
sll0593		glucokinase	6							
slr0329		glucokinase	6							
sll0745		phosphofructokinase	6	0.044 / 0.029		-0,4			-0,51	
sll1275		pyruvate kinase 2	6							
6,3	Energy metabolism / Pentose phospate pathway		6							

sll0807	rpe	pentose-5-phosphate-3-epimerase	6							
sll1709		3-ketoacyl-acyl carrier protein reductase	6							
slr0884	gap1	glyceraldehyde 3-phosphate dehydrogenase 1 (NAD+)	6	0,002						-1,06
sll0920	ppc	phosphoenolpyruvate carboxylase	6							
slr1734	opcA	glucose 6-phosphate dehydrogenase assembly protein	6							
sll1479		6-phosphogluconolactonase	6							
slr1793		transaldolase	6							
sll1070		transketolase	6							
6,4	Energy metabolism / Pyruvate and acetyl-CoA metabolism		6							
slr0301		phosphoenolpyruvate synthase	6							
slr2132		phosphotransacetylase	6							
slr0091		aldehyde dehydrogenase	6							
slr1096		dihydrolipoamide dehydrogenase	6							
sll1299		acetate kinase	6							
sll0542		acetyl-coenzyme A synthetase	6	0.008 / 0.037				-0,29		0,3
sll1019		hydroxyacylglutathione hydrolase	6							
slr0721		malic enzyme	6							
6,5	Energy metabolism / Pyruvate dehydrogenase		6							
sll1841		pyruvate dehydrogenase dihydrolipoamide acetyltransferase component (E2)	6							
sll1721		pyruvate dehydrogenase E1 component, beta subunit	6	0.035 / 0.043				-0,56		0,33
sll0587		pyruvate kinase	6							
slr1934		pyruvate dehydrogenase E1 component, alpha subunit	6	0,045					-0,75	
6,6	Energy metabolism / Sugars		6							
slr0194	rpiA	ribose 5-phosphate isomerase	6	0,042					-0,93	
sll1212		GDP-mannose 4,6-dehydratase	6	0.027/0.043					-0,97	1,11
slr1166		UDP-glucose:tetrahydrobiopterin glucosyltransferase	6							
slr0493		similar to mannose-1-phosphate guanylyltransferase	6							
slr0953		sucrose-phosphate phosphatase	6	0,031				-0,9		
sll1370	rfbM	mannose-1-phosphate guanylyltransferase	6							
sll0045	spsA	sucrose phosphate synthase	6	0,044	-0,97					
slr1617		similar to UDP-glucose 4-epimerase	6							
slr1078		similar to UDP-glucose 4-epimerase	6	0,003				-0,47		
ssl2153		probable ribose phosphate isomerase B	6							
slr1299		UDP-glucose dehydrogenase	6							
sll1496		mannose-1-phosphate guanyltransferase	6							
sll1558		mannose-1-phosphate guanyltransferase	6							
slr0942		alcohol dehydrogenase [NADP+]	6							
slr1448		fructokinase	6							
sll1231		mannosyltransferase	6							
sll1538		similar to beta-hexosaminidase a precursor	6	0,021						-0,23
slr2074		similar to mannose-1-phosphate guanylyltransferase	6							
slr1067		UDP-glucose 4-epimerase	6							
sll0244		UDP-glucose 4-epimerase	6							
6,7	Energy metabolism / TCA cycle		6							
sll1557		succinyl-CoA synthetase alpha chain	6							
slr1233		succinate dehydrogenase flavoprotein subunit	6							
slr1289	icd	isocitrate dehydrogenase (NADP+)	6	0,031				-0,67		
sll0401		citrate synthase	6							
slr0018		fumarase	6							
sll0891		malate dehydrogenase	6							
sll0823		probable succinate dehydrogenase iron-sulfur protein	6							
sll1625		succinate dehydrogenase iron- sulphur protein subunit	6							
sll1023		succinyl-CoA synthetase beta chain	6							
7,1	Fatty acid, phospholipid and sterol metabolism		7							
sll0053	accC	biotin carboxylase	7							
ssl2084	acpP	acyl carrier protein	7							
sll1441	desB	acyl-lipid desaturase (omega-3)	7	0,001				-0,56		
sll0541	desC,des9	acyl-lipid desaturase (delta 9)	7							
sll0262	desD	acyl-lipid desaturase (delta 6)	7	0,025				-0,55		
slr1020	sqdB	sulfolipid biosynthesis protein SqdB	7							
sll1605		(3R)-hydroxymyristol acyl carrier protein dehydrase	7							
slr0886		3-oxoacyl-[acyl-carrier protein] reductase	7	0,023					-0,9	
sll1069		3-oxoacyl-[acyl-carrier-protein] synthase II	7							
slr1051		enoyl-[acyl-carrier-protein] reductase	7							
sll1655		similar to biotin [acetyl-CoA-carboxylase] ligase	7	0,006				-1,24		
slr0776		UDP-3-o-[3-hydroxymyristoyl] glucosamine n-acyltransferase	7							
slr1755		NAD+ dependent glycerol-3-phosphate dehydrogenase	7							
slr2033	rubA	membrane-associated rubredoxin, essential for photosystem I assembly	7							
slr1993	phaA	PHA-specific beta-ketothiolase	7							

slr0054		diacylglycerol kinase	7							
slr2089	shc	squalene-hopene-cyclase	7	0,010					-0,23	
slr0089		gamma-tocopherol methyltransferase	7							
sll0330		sepiapterine reductase	7	0,017						1,11
slr1369	cdsA	phosphatidate cytidylyltransferase	7							
slr1510	plsX	fatty acid/phospholipid synthesis protein PlsX	7							
sll0336	accD, ycf1	acetyl-CoA carboxylase beta subunit	7							
slr1511	fabH	3-oxoacyl-[acyl-carrier-protein] synthase III	7							
slr1167	gldA	glycerol dehydrogenase	7	0,008				-0,46		
sll1085	glpD	glycerol-3-phosphate dehydrogenase	7							
sll1522		CDP-diacylglycerol--glycerol-3-phosphate 3-phosphatidyltransferase	7							
slr0224		similar to sterol C5-desaturase	7							
sll0728	accA	acetyl-CoA carboxylase alpha subunit	7	0.034 / 0.042					-0,33	0,38
slr0435	accB	biotin carboxyl carrier protein of acetyl-CoA carboxylase	7	0,026				0,44		
slr1350	desA	acyl-lipid desaturase (delta 12)	7							
slr2023	fabD	malonyl coenzyme A-acyl carrier protein transacylase	7	0,011		-0,38				
slr1672	glpK	glycerol kinase	7							
slr1994	phaB	PHA-specific acetoacetyl-CoA reductase	7							
slr0384	sqdX	sulfoquinovosyldiacylglycerol biosynthesis protein SqdX	7	0,020			-0,09			
slr1609		long-chain-fatty-acid CoA ligase	7							
slr0574		cytochrome P450	7							
slr1332		beta ketoacyl-acyl carrier protein synthase	7							
sll0418		2-methyl-6-phytylbenzoquinone methyltransferase	7							
slr2124		3-oxoacyl-[acyl-carrier protein] reductase	7							
8,1	Photosynthesis and respiration / ATP synthase		8							
sll1326	atpA	ATP synthase alpha chain	8	0,026						0,47
slr1329	atpB	ATP synthase beta subunit	8							
sll1327	atpC	ATP synthase gamma chain	8							
sll1325	atpD	ATP synthase delta chain of CF(1)	8							
slr1330	atpE	ATP synthase epsilon chain of CF(1)	8							
sll1324	atpF	ATP synthase B chain (subunit I) of CF(0)	8							
sll1323	atpG	ATP synthase subunit b' of CF(0)	8							
ssl2615	atpH	ATP synthase C chain of CF(0)	8							
sll1322	atpI	ATP synthase A chain of CF(0)	8							
sll1321		hypothetical protein	8	0,019					-0,72	
8,2	Photosynthesis and respiration / CO2 fixation		8							
sll1028	ccmK2	carbon dioxide concentrating mechanism protein CcmK	8	0.034 / 0.03			-0,34		-0,36	
slr1839	ccmK4	carbon dioxide concentrating mechanism protein CcmK homolog 4, putative carboxysome assembly protein	8							
sll1031	ccmM	carbon dioxide concentrating mechanism protein CcmM, putative carboxysome structural protein	8	0,013	0,5					
sll1342	gap2	NAD(P)-dependent glyceraldehyde-3-phosphate dehydrogenase	8							
sll1525	prk	phosphoribulokinase	8							
slr0009	rbcL	ribulose bisphosphate carboxylase large subunit	8							
slr0012	rbcS	ribulose bisphosphate carboxylase small subunit	8	0.013 / 0.036					-0,46	0,79
sll1029	ccmK1	carbon dioxide concentrating mechanism protein CcmK	8							
sll1030	ccmL	carbon dioxide concentrating mechanism protein CcmL, putative carboxysome assembly protein	8							
slr0436	ccmO	carbon dioxide concentrating mechanism protein CcmO	8	0,046						-0,31
sll0934	ccmA	carboxysome formation protein CcmA	8							
slr1838	ccmK3	carbon dioxide concentrating mechanism protein CcmK homolog 3, putative carboxysome assembly protein	8							
slr0783	tpi	triosephosphate isomerase	8							
slr0051	ecaB	periplasmic beta-type carbonic anhydrase	8	0,012		0,17				-0,75
slr1347		beta-type carbonic anhydrase localized in the carboxysome	8							
8,3	/ Photosynthesis and respiration / Cytochrome b6/f complex		8							
sll1317	petA	apocytochrome f, component of cytochrome b6/f complex	8	0,021				-0,61		
slr0342	petB	cytochrome b6	8							
sll1316	petC1	cytochrome b6-f complex iron-sulfur subunit (Rieske iron sulfur protein)	8							
slr0343	petD	cytochrome b6-f complex subunit 4	8							
smr0003	petM	cytochrome b6-f complex subunit PetM	8	0,029				0,79		
sll1182	petC3	cytochrome b6-f complex alternative iron-sulfur subunit (Rieske iron sulfur protein)	8							
slr1185	petC2	cytochrome b6-f complex alternative iron-sulfur subunit (Rieske iron sulfur protein)	8							
smr0010	petG	cytochrome b6-f complex subunit 5	8							
sml0004	petN	cytochrome b6-f complex subunit VIII	8							

8,4	Photosynthesis and respiration / NADH dehydrogenase		8							
sll0519	ndhA	NADH dehydrogenase subunit 1	8							
sll0223	ndhB	NADH dehydrogenase subunit 2	8	0.005 / 0.044			-0,6		-0,58	
sll0027	ndhD4	NADH dehydrogenase subunit 4 (involved in constitutive, low affinity CO2 uptake)	8							
sll0522	ndhE	NADH dehydrogenase subunit 4L	8							
slr0844	ndhF1	NADH dehydrogenase subunit 5	8							
sll0026	ndhF4	NADH dehydrogenase subunit 5 (involved in constitutive, low affinity CO2 uptake)	8							
slr1279	ndhC	NADH dehydrogenase subunit 3	8							
slr1281	ndhJ	NADH dehydrogenase subunit I	8							
slr1280	ndhK	NADH dehydrogenase subunit NdhK	8							
slr0851	ndbA	type 2 NADH dehydrogenase	8							
slr1743	ndbB	type 2 NADH dehydrogenase NdbB	8							
slr1291	ndhD2	NADH dehydrogenase subunit 4	8							
slr0331	ndhD1	NADH dehydrogenase subunit 4 (involved in photosystem-1 cyclic electron flow)	8							
sll0521	ndhG	NADH dehydrogenase subunit 6	8							
sll0520	ndhI	NADH dehydrogenase subunit NdhI	8							
sll1484	ndbC	type 2 NADH dehydrogenase	8							
sll1733	ndhD3	NADH dehydrogenase subunit 4 (involved in low CO2-inducible, high affinity CO2 uptake)	8							
slr2007	ndhD5	NADH dehydrogenase subunit 4	8	0,003						3,34
slr2009	ndhD6	NADH dehydrogenase subunit 4	8							
sll1732	ndhF3	NADH dehydrogenase subunit 5 (involved in low CO2-inducible, high affinity CO2 uptake)	8							
slr0261	ndhH	NADH dehydrogenase subunit 7	8	0,024						0,33
ssr1386	ndhL	NADH dehydrogenase subunit NdhL	8							
8,5	Photosynthesis and respiration / Photosystem I		8							
sll0634	btpA	photosystem I biogenesis protein BtpA	8							
ssl0563	psaC	photosystem I subunit VII	8							
slr0737	psaD	photosystem I subunit II	8	0,017				0,58		
ssr2831	psaE	photosystem I subunit IV	8							
sll0819	psaF	photosystem I reaction center subunit III precursor (PSI-F), plastocyanin (cyt c553) docking protein	8							
smr0004	psaI	photosystem I subunit VIII	8	0,043						-0,47
sml0008	psaJ	photosystem I subunit IX	8							
ssr0390	psaK1	photosystem I reaction center subunit X	8	0,047		0,51				
sll0629	psaK2	alternative photosystem I reaction center subunit X	8							
slr1655	psaL	photosystem I subunit XI	8							
slr1834	psaA	P700 apoprotein subunit Ia	8							
slr1835	psaB	P700 apoprotein subunit Ib	8							
smr0005	psaM	photosystem I subunit XII	8							
slr0171	ycf37	photosystem I assembly related protein Ycf37	8							
sll0226	ycf4	photosystem I assembly related protein	8							
slr0823	ycf3	photosystem I assembly related protein	8							
8,6	Photosynthesis and respiration / Photosystem II		8							
sll0247	isiA	iron-stress chlorophyll-binding protein, homologous to psbC (CP43)	8	0,034					0,95	
slr1645	psb27, psb	photosystem II 11 kD protein	8							
slr0906	psbB	photosystem II core light harvesting protein	8							
slr0927	psbD2	photosystem II reaction center D2 protein	8							
ssr3451	psbE	cytochrome b559 alpha subunit	8	0,024						-0,41
sml0005	psbK	photosystem II PsbK protein	8							
sll0427	psbO	photosystem II manganese-stabilizing polypeptide	8	0,029				0,69		
sll1418	psbP2	photosystem II oxygen-evolving complex 23K protein PsbP homolog	8							
sll0258	psbV	cytochrome c550	8							
slr2034	ycf48	putative homolog of plant HCF136, which is essential for stability or assembly of photosystem II	8	0,013						0,48
sll0851	psbC	photosystem II CP43 protein	8							
sll0849	psbD	photosystem II reaction center D2 protein	8							
sll1398	psb28, psb	photosystem II reaction center 13 kDa protein	8							
ssl2598	psbH	photosystem II PsbH protein	8	0,027				1,35		
smr0008	psbJ	photosystem II PsbJ protein	8							
sll1194	psbU	photosystem II 12 kDa extrinsic protein	8	0,039			0,34			
slr1739	psb28-2	photosystem II 13 kDa protein homolog	8							
smr0009	psbN	photosystem II PsbN protein	8							
slr1181	psbA1	photosystem II D1 protein	8							
slr1311	psbA2	photosystem II D1 protein	8	0,032				1,09		
sll1867	psbA3	photosystem II D1 protein	8	0,031				1,34		
smr0006	psbF	cytochrome b559 b subunit	8	0,048			0,24			
sml0001	psbI	photosystem II reaction center PsbI protein	8							
smr0007	psbL	photosystem II PsbL protein	8							
sml0003	psbM	photosystem II reaction center M protein	8	0,037				2,62		
smr0001	psbT, ycf8	photosystem II PsbT protein	8	0,003				1,1		
sml0002	psbX	photosystem II PsbX protein	8							
sml0007	psbY	photosystem II protein Y	8							
8,7	Photosynthesis and respiration / Phycobilisome		8							
ssr3383	apcC	phycobilisome small core linker polypeptide	8							

slr0335	apcE	phycobilisome core-membrane linker polypeptide	8							
sll1578	cpcA	phycocyanin alpha subunit	8							
sll1577	cpcB	phycocyanin beta subunit	8							
sll1580	cpcC1	phycobilisome rod linker polypeptide	8							
sll1579	cpcC2	phycobilisome rod linker polypeptide	8							
ssl3093	cpcD	phycobilisome small rod linker polypeptide	8							
sll1471	cpcG2	phycobilisome rod-core linker polypeptide	8	0.03/0.004/0.023/0.03		1,76			3,58	2,17
slr2067	apcA	allophycocyanin alpha subunit	8							
slr1986	apcB	allophycocyanin beta subunit	8	0,008				0,3		
sll0928	apcD	allophycocyanin-B	8							
slr1459	apcF	phycobilisome core component	8							
slr2051	cpcG1	phycobilisome rod-core linker polypeptide	8							
ssl0452	nblA1	phycobilisome degradation protein NblA	8							
ssl0453	nblA2	phycobilisome degradation protein NblA	8							
slr1878	cpcE	phycocyanin alpha-subunit phycocyanobilin lyase	8							
sll1051	cpcF	phycocyanin alpha-subunit phycocyanobilin lyase	8							
sll1663		phycocyanin alpha phycocyanobilin lyase related protein	8							
8,8	Photosynthesis and respiration / Respiratory terminal oxidases		8							
sll1899	ctaB	cytochrome c oxidase folding protein	8							
sll0813	ctaC	cytochrome c oxidase subunit II	8	0,027					0,22	
slr2083	ctaEII	cytochrome c oxidase subunit III	8							
slr1137	ctaDI	cytochrome c oxidase subunit I	8							
slr2082	ctaDII	cytochrome c oxidase subunit I	8							
slr1136	ctaCI	cytochrome c oxidase subunit II	8	0,030						-0,23
slr1138	ctaEI	cytochrome c oxidase subunit III	8	0,004						-0,53
slr1379	cydA	quinol oxidase subunit I	8							
slr1380	cydB	quinol oxidase subunit II	8							
8,9	Photosynthesis and respiration / Soluble electron carriers		8							
sll1796	petJ	cytochrome c553	8							
sll0248	isiB	flavodoxin	8	0,015				-0,6		
sll1584		ferredoxin like protein	8							
slr0150	petF, fdx	ferredoxin, petF-like protein	8	0,014					1,1	
ssl3044		probable ferredoxin	8	0,032						0,98
slr1643	petH	ferredoxin-NADP oxidoreductase	8							
ssl2559		ferredoxin	8							
ssl0020	petF	ferredoxin I, essential for growth	8							
slr2059		iron-sulfur cluster binding protein homolog	8	0,035						-0,19
sll1382	petF, fdx	ferredoxin, petF-like protein	8							
ssr3184		4Fe-4S type iron-sulfur protein	8							
sll0741		pyruvate flavodoxin oxidoreductase	8							
sll1245	cytM	cytochrome cM	8	0,030					-0,75	
sll0199	petE	plastocyanin	8							
slr1828	petF, fdx	ferredoxin, petF-like protein	8							
9,1	Purines, pyrimidines, nucleosides, and nucleotides / Interconversi		9							
sll1258		dCTP deaminase	9							
sll1852		nucleoside diphosphate kinase	9	0,030						1,43
sll1635		Thy1 protein homolog	9							
9,2	Purines, pyrimidines, nucleosides, and nucleotides / Purine ribonu		9							
sll1815	adk	adenylate kinase	9							
sll1059		adenylate kinase	9	0,046				-0,81		
sll1035		uracil phosphoribosyltransferase	9							
sll1823	purA	adenylosuccinate synthetase	9							
slr1226	purC	phosphoribosyl aminoidazole succinocarboxamide synthetase	9							
sll0469		ribose-phosphate pyrophosphokinase	9	0,012				0,89		
sll0398		deoxyguanosinetriphosphate triphosphohydrolase	9	0,025						-0,55
sll0578	purK	phosphoribosylaminoimidazole carboxylase ATPase subunit	9							
sll1430		adenine phosphoribosyltransferase	9							
slr0520	purL	phosphoribosyl formylglycinamidine synthase	9							
slr0861	purT	glycinamide ribonucleotide transformylase	9	0,021						0,52
slr1123		guanylate kinase	9							
slr1722		inosine-5'-monophosphate dehydrogenase	9							
slr0213	guaA	GMP synthetase	9							
sll0421	purB	adenylosuccinate lyase	9	0.013/0.014/0.030		-0,3			-0,89	0,47
slr1159	purD	glycinamide ribonucleotide synthetase	9							
sll0901	purE	phosphoribosylaminoimidazole carboxylase	9							
sll0757	purF	amidophosphoribosyltransferase	9							
slr0597	purH	phosphoribosyl aminoimidazole carboxy formyl formyltransferase/inosinemonophosphate cyclohydrolase (PUR-H(J))	9	0.014 / 0.024						0,53
sll1056	purL	phosphoribosylformyl glycinamidine synthetase II	9							
slr0838	purM	phosphoribosyl formylglycinamidine cyclo-ligase	9	0,045						0,65
slr0477	purN	phosphoribosylglycinamide formyltransferase	9							
sll1776		deoxyribose-phosphate aldolase	9							
slr0591		ribonucleoside-diphosphate reductase beta chain	9	0,035					-0,61	
sll0368		uracil phosphoribosyltransferase	9							
9,3	Purines, pyrimidines, nucleosides, and nucleotides / Pyrimidine ril		9							

sll0144	pyrH	uridine monophosphate kinase	9							
slr1164		ribonucleotide reductase subunit alpha	9							
slr1418	pyrD	dihydroorotate dehydrogenase	9							
slr0406	pyrC	dihydroorotase	9							
sll0838	pyrF	orotidine 5' monophosphate decarboxylase	9	0,036					-0,34	
sll1443	pyrG	CTP synthetase	9	0,047						1,16
sll0070	purU	phosphoribosylglycinamide formyltransferase	9							
slr1476	pyrB	aspartate carbamoyltransferase	9							
sll1018	pyrC	dihydroorotase	9							
slr1237		cytosine deaminase	9							
slr0185		orotate phosphoribosyltransferase	9							
sll1631		putative cytidine and deoxycytidylate deaminase	9							
sll0509		similar to 5',5'''-P-1,P-4-tetraphosphate phosphorylase II	9							
10,1	Regulatory functions		10							
slr1783	ycf29	two-component response regulator NarL subfamily	10							
sll1626		LexA repressor	10	0,036						-0,61
slr1234		protein kinase C inhibitor	10							
sll1286		transcriptional regulator	10							
slr2024		two-component response regulator CheY subfamily	10							
slr1693		two-component response regulator PatA subfamily	10							
slr0474	rcp1	two-component response regulator CheY subfamily, regulator for phytochrome 1 (Cph1)	10							
sll1005		MazG protein homolog	10							
slr0527		transcription regulator ExsB homolog	10							
sll0594		transcriptional regulator	10							
slr0473	cph1, hik3	cyanobacterial phytochrome 1, two-component sensor histidine kinase	10	0,042					0,88	
sll1742	nusG	transcription antitermination protein NusG	10							
slr0240		transcriptional regulator	10	0,035						0,42
sll0485		two-component response regulator NarL subfamily	10							
slr1584		two-component transcription regulator OmpR subfamily	10							
sll0567	fur	ferric uptake regulation protein	10							
slr0210	hik9	two-component sensor histidine kinase	10							
slr1324	hik23	two-component hybrid sensor and regulator	10							
slr0222	hik25	two-component hybrid sensor and regulator	10	0,049	-0,53					
slr0640	hik27	two-component sensor histidine kinase	10							
sll1296	hik39	two-component hybrid sensor and regulator	10							
sll1387	pppA	serine/threonine protein phosphatase PppA	10	0,013				-0,23		
sll0690		probable transcription regulator	10							
slr1738		transcription regulator Fur family	10	0,028						0,88
slr0741		transcriptional regulator	10	0,009						-0,35
slr1042		two-component response regulator CheY subfamily	10	0,003						-0,39
slr1594		two-component response regulator PatA subfamily	10							
sll1291		two-component response regulator PatA subfamily	10							
sll1672	hik12	two-component hybrid sensor and regulator	10							
slr0947	rpaB, ycf27	response regulator for energy transfer from phycobilisomes to photosystems	10	0.004 / 0.039		0,08		0,7		
sll1371	sycrp1	cAMP receptor protein, essential for motility	10							
slr0724		HtaR suppressor protein homolog	10	0,043				0,48		
slr1212		similar to two-component sensor histidine kinase	10							
sll0782		transcriptional regulator	10							
sll1673		two-component response regulator	10							
slr2100		two-component response regulator	10							
slr1213		two-component response regulator AraC subfamily	10							
sll0030	cmpR	cmp operon transcriptional regulator, LysR family protein	10							
sll0750	hik8, sasA	two-component sensor histidine kinase, KaiC-interacting protein, involved in circadian rhythm	10							
sll1590	hik20	two-component sensor histidine kinase	10							
sll0790	hik31	two-component sensor histidine kinase	10							
slr1285	hik34	two-component sensor histidine kinase	10	0,022		0,52				
slr2099	hik40	two-component hybrid sensor and regulator	10							
sll1555	hik42	two-component hybrid sensor and regulator	10							
slr0322	hik43	two-component hybrid sensor and regulator	10	0,044					-0,31	
sll1594	ndhR	ndhF3 operon transcriptional regulator, LysR family protein	10							
sll1575	spkA	a part of spkA: serine/threonine protein kinase, regulates cellular motility (disrupted by frameshift mutation)	10							
slr0321		GTP-binding protein ERA homolog	10							
sll1383		probable myo-inositol-1(or 4)-monophosphatase	10							
slr1225		serine/threonine kinase	10							
slr0599		serine/threonine kinase	10	0,001				-1,14		
slr1443		serine/threonine kinase	10							
slr0152		serine/threonine protein kinase	10	0,002				0,49		
slr1416		similar to MorR protein	10							
sll1957		transcriptional regulator	10							
slr1305		two-component response regulator	10	0,037			-0,38			

sll1292		two-component response regulator CheY subfamily	10								
sll1708		two-component response regulator NarL subfamily	10								
sll1544		two-component response regulator NarL subfamily	10								
sll0789		two-component response regulator OmpR subfamily	10								
slr1041		two-component response regulator PatA subfamily	10								
sll1334		two-component sensor histidine kinase	10								
sll1330		two-component system response regulator OmpR subfamily	10	0,011				1,27			
slr1588		two-component transcription regulator	10								
slr1860	icfG	carbon metabolisms regulatory protein IcfG	10								
sll1423	ntcA, ycf28	global nitrogen regulator	10								
sll0776	spkD	serine/threonine kinase	10								
sll1408		transcriptional regulator	10								
sll0649		two-component response regulator OmpR subfamily	10								
slr1414	hik11	two-component sensor histidine kinase	10								
slr2104	hik22	two-component hybrid sensor and regulator	10								
sll1475	hik32	a part of phytochrome-like sensor histidine kinase gene (disrupted by insertion of IS)	10								
slr0073	hik36	two-component sensor histidine kinase	10								
sll0792	ziaR	Zinc-responsive repressor ZiaR	10								
sll2014		sugar fermentation stimulation protein	10	0,045			-0,05				
slr1489		transcriptional regulator	10								
slr0312		two-component response regulator NarL subfamily	10								
slr1991	cya1	adenylate cyclase	10								
sll0646	cya2	guanylyl cyclase	10								
slr1393	hik1	phytochrome-like protein, two-component sensor histidine kinase	10								
slr1147	hik2	two-component sensor histidine kinase	10	0,023		-0,41					
sll1228	hik4	two-component hybrid sensor and regulator	10								
sll1888	hik5	two-component sensor histidine kinase	10								
sll1871	hik6	two-component system sensory histidine kinase	10	0,015		-0,54					
slr0533	hik10	two-component sensor histidine kinase	10								
sll1003	hik13	two-component sensor histidine kinase	10								
slr1759	hik14	two-component hybrid sensor and regulator	10	0,043			-0,56				
sll1353	hik15	two-component sensor histidine kinase	10								
slr1805	hik16	two-component sensor histidine kinase	10								
sll1905	hik19	two-component hybrid sensor and regulator	10								
slr2098	hik21	two-component hybrid sensor and regulator	10								
slr1969	hik24	two-component sensor histidine kinase	10	0,003							-0,86
slr0484	hik26	two-component sensor histidine kinase	10								
sll0474	hik28	two-component hybrid sensor and regulator	10								
slr0311	hik29	two-component sensor histidine kinase	10	0.027 / 0.004	-0,47						-0,5
sll0094	hik37	two-component sensor histidine kinase	10								
slr1400	hik38	two-component hybrid sensor and regulator	10								
sll1229	hik41	two-component hybrid sensor and regulator	10								
sll0797	nrsR,rppA	redox-responsive and/or Ni(II)-responsive regulator, two-component response regulator OmpR subfamily	10	0,005					-0,53		
sll0798	nrsS,rppB,	Ni(II)-sensor and/or redox sensor, two-component sensor histidine kinase	10								
sll0337	phoR, hik7	phosphate sensor, two-component sensor histidine kinase	10								
sll0038	pixG, pisG	positive phototaxis protein, two-component response regulator PatA subfamily	10	0,021		0,34					
sll0039	pixH, pisH	positive phototaxis protein, two-component response regulator CheY subfamily	10								
sll0043	pixL, taxA'	positive phototaxis protein, homologous to chemotaxis protein CheA, two-component hybrid histidine kinase	10								
sll1124	plpA, hik3	two-component sensor histidine kinase, phytochrome-like protein	10								
sll1771	pphA	protein serin-threonin phosphatase	10								
slr0115	rpaA, ycf2	response regulator for energy transfer from phycobilisomes to photosystems	10								
sll1574	spkA'	a part of spkA: serine/threonine protein kinase, regulates cellular motility (disrupted by frameshift mutation)	10								
sll1924	sycrp2	cAMP receptor protein sycrp1 homolog	10								
sll0998	ycf30	LysR family transcriptional regulator	10								
sll1879	ycf55	two-component response regulator	10								
slr1694		expression activator appA homolog	10	0,041							-0,7
sll1937		ferric uptake regulation protein	10	0,041							-0,47
slr1325		GTP pyrophosphokinase	10	0.028 / 0.025					-0,54		0,24
slr1090		GTP-binding protein	10								
sll1670		heat-inducible transcription repressor HrcA homolog	10								
sll1329		inositol monophosphate family protein	10								
slr0835		MoxR protein homolog	10								
slr1975		N-acylglucosamine 2-epimerase	10								
slr1666		pleiotropic regulatory protein homolog	10								
sll1161		probable adenylate cyclase	10								

slr0449		probable transcriptional regulator	10	0,032							-0,26
slr0687		probable two-component response regulator	10								
slr2041		probable two-component response regulator	10	0,003		-0,2					
slr0418		putative transcripton factor DevT homolog	10	0,029							0,41
slr1697		serine/threonine kinase	10								
slr1871		transcriptional regulator	10								
slr1245		transcriptional regulator	10								
sll1205		transcriptional regulator	10								
ssl0564		transcriptional regulator	10								
slr0701		transcriptional regulator	10	0,036							-1,18
sll1392		transcriptional regulator	10	0.001 / 0.049					0,49	0,96	
slr0895		transcriptional regulator	10								
sll1872		transcriptional regulator	10								
slr1983		two-component hybrid sensor and regulator	10								
slr1760		two-component response regulator	10								
sll1624		two-component response regulator	10	0,008					-0,6		
slr1037		two-component response regulator CheY subfamily	10								
slr1982		two-component response regulator CheY subfamily	10								
sll0921		two-component response regulator NarL subfamily	10								
sll1592		two-component response regulator NarL subfamily	10								
slr1909		two-component response regulator NarL subfamily	10								
sll0396		two-component response regulator OmpR subfamily	10								
slr0081		two-component response regulator OmpR subfamily	10								
slr1214		two-component response regulator PatA subfamily	10								
slr1837		two-component system response regulator OmpR subfamily	10								
11,1	DNA replication, restriction, modification, recombination, and repa		11								
slr1689	fpg	formamidopyrimidine-DNA glycosylase	11	0,039	0,45						
slr1536	recQ	ATP-dependent DNA helicase RecQ	11	0,007					0,35		
sll2005	gyrB	DNA gyrase B subunit [Contains: Ssp gyrB intein]	11								
slr0915		putative endonuclease	11								
sll0766	radC	DNA repair protein RadC	11								
slr0020	recG	DNA recombinase	11								
slr1844	uvrA	excinuclease ABC subunit A	11	0.039 / 0.020						-1,06	-0,7
slr0603	dnaE	DNA polymerase III alpha subunit [Contains: Ssp dnaE intein]	11								
sll0896	ruvC	Holliday juction resolvase RuvC	11								
sll0459	uvrB	excinuclease ABC subunit B	11	0,002					-0,28		
slr1597		chromosome partitioning ATPase, ParA family	11								
slr0446	dnaX	DNA polymerase III delta' subunit	11								
sll1209	lig	DNA ligase	11								
sll1354	recJ	single-strand-DNA-specific exonuclease RecJ	11	0.0001/0.003	-0,4				0,28		
sll0613	ruvB	Holliday junction DNA helicase RuvB	11	0,018			-0,18				
slr0925	ssb	single-stranded DNA-binding protein	11	0,035					0,42		
slr2058	topA	DNA topoisomerase I	11								
slr1822		endonuclease III	11	0,022							-0,25
sll0377		transcription-repair coupling factor	11								
sll1868	dnaG	DNA primase	11								
sll0569	recA	RecA gene product	11								
sll1520	recN	DNA repair protein RecN	11								
sll0729		probable DNA methyltransferase	11								
sll0709		putative endonuclease	11								
slr0965	dnaN	DNA polymerase III beta subunit	11								
sll0848	dnaA	chromosomal replication initiator protein DnaA	11								
slr0833	dnaB	replicative DNA helicase [Contains: Ssp dnaB intein]	11	0,008							-0,48
sll1572	dnaE	DNA polymerase III alpha subunit [Contains: Ssp dnaE intein]	11								
sll1360	dnaX	DNA polymerase III subunit gamma/tau [Contains: Ssp dnaX intein]	11	0,043							-0,42
slr0417	gyrA	DNA gyrase subunit A	11								
sll1941	gyrA	DNA gyrase A subunit	11								
slr1199	mutL	DNA mismatch repair protein MutL	11								
sll1772	mutS	DNA mismatch repair protein MutS	11	0.041 / 0.015		-0,88				-1,33	
sll1143	pcrA	ATP-dependent helicase PcrA	11								
slr0854	phrA	DNA photolyase	11								
slr0707	polA	DNA polymerase I	11	0,039							0,57
slr0448	radA	DNA repair protein RadA	11								
sll1277	recF	RecF protein	11								
slr1426	recR	recombination protein RecR	11								
sll0876	ruvA	Holliday junction DNA helicase RuvA	11								
slr1322	tldD	putative modulator of DNA gyrase; TldD	11								
sll0865	uvrC	excinuclease ABC subunit C	11	0,043					-1,6		
slr1803		adenine-specific DNA metylase	11	0,019							-0,69
sll1629		bacterial cryptochrome	11								
slr0929		chromosome partitioning protein, ParA family	11								
slr0214		cytosine-specific methyltransferase(5'-CGATCG-3')	11								
sll1165		DNA mismatch repair protein	11								
slr1543		DNA-damage-inducible protein F	11								
sll1854		exodeoxyribonuclease III	11								
slr0733		integrase-recombinase protein	11								

slr1134		mutator MutT homolog	11							
slr0920		mutator MutT protein	11							
		mutator MutT protein	11							
sll0270		primosomal protein N'	11							
sll0021		probable exonuclease	11							
slr0451		putative helicase	11							
sll0887		putative modulator of DNA gyrase; PmbA homolog	11							
sll1366		putative SNF2 helicase	11							
sll1537		similar to mutator MutT protein	11	0,016						0,61
slr0790		similar to ultraviolet light resistance protein B	11							
12,1	Transcription / Degradation of RNA		12							
slr1130	rhnB	ribonuclease HII	12							
slr1469	rnpA	protein subunit of ribonuclease P (RNase P)	12							
slr0080	rnhA	ribonuclease H	12	0,028	-0,69					
sll0320		probable ribonuclease D	12							
slr0346	rnc	ribonuclease III	12	0.027 / 0.026				0,45		-0,24
slr1129	rne	ribonuclease E	12							
sll1290		probable ribonuclease II	12							
12,2	RNA synthesis, modification, and DNA transcription		12							
sll1789	rpoC2	RNA polymerase beta prime subunit	12							
slr1859		anti-sigma f factor antagonist	12							
slr0743		similar to N utilization substance protein	12	0,003			-0,3			
slr1265	rpoC1	RNA polymerase gamma-subunit	12							
slr1646	rnc	ribonuclease III	12							
sll1818	rpoA	Transcription RNA polymerase alpha subunit	12							
slr1856		phosphoprotein substrate of icfG gene cluster	12							
sll1043		polyribonucleotide nucleotidyltransferase	12							
ssr1600		similar to anti-sigma f factor antagonist	12							
sll0306	sigB	RNA polymerase group 2 sigma factor	12							
sll0856	sigH	RNA polymerase ECF-type (group 3) sigma-E factor	12	0,022						0,21
slr1912		putative PP2C-type protein phosphatase	12							
slr0083	crhR	RNA helicase Light	12							
sll0184	sigC	group2 RNA polymerase sigma factor SigC	12							
slr1545	sigG	RNA polymerase ECF-type (group 3) sigma-E factor	12							
slr1861		probable sigma regulatory factor	12							
sll1787	rpoB	RNA polymerase beta subunit	12							
slr0653	sigA,rpoD	principal RNA polymerase sigma factor SigA	12	0.008 / 0.006					-0,57	-0,36
sll2012	sigD	group2 RNA polymerase sigma factor SigD	12							
sll1689	sigE,rpoD2	group2 RNA polymerase sigma factor SigE	12	0,024						-1,04
slr1564	sigF	group 3 RNA polymerase sigma factor	12							
sll0687	sigI	RNA polymerase ECF-type (group 3) sigma factor	12							
sll0271		N utilization substance protein B homolog	12							
13,1	Translation / Aminoacyl tRNA synthetases and tRNA modification		13							
sll1074	leuS	leucyl-tRNA synthetase	13							
slr1550	lysS	lysyl-tRNA synthetase	13	0.012 / 0.025					-0,71	0,34
slr1703	serS	seryl-tRNA synthetase	13							
slr0713	tgt	tRNA-guanine transglycosylase	13	0,003	0,53					
slr1031	tyrS	tyrosyl tRNA synthetase	13							
slr0557	valS	valyl-tRNA synthetase	13							
slr0877		glutamyl-tRNA(Gln) amidotransferase subunit A	13	0,013	0,33					
sll1435		glutamyl-tRNA(Gln) amidotransferase subunit B	13							
sll1098	fus	elongation factor EF-G	13	0,031					-0,41	
sll1362	ileS	isoleucyl-tRNA synthetase	13							
slr0649	metS	methionyl-tRNA synthetase	13							
sll0454	pheS	phenylalanyl-tRNA synthetase alpha chain	13							
slr0033		glutamyl-tRNA(Gln) amidotransferase subunit C	13							
sll0927		S-adenosylmethionine synthetase	13	0,033			0,34			
sll1198		tRNA (guanine-N1)-methyltransferase	13							
sll1820		tRNA pseudouridine synthase 1	13							
slr0638	glyQ	glycyl-tRNA synthetase alpha chain	13							
slr0120		probable tRNA/rRNA methyltransferase	13	0,029				-1,2		
sll0817		tRNA delta-2-isopentenylpyrophosphate (IPP) transferase	13							
sll0362	alaS	alanyl-tRNA synthetase	13	0,047				-0,37		
sll0502	argS	arginyl-tRNA-synthetase	13	0,040					-0,67	
sll0495	asnS	asparaginyl-tRNA synthetase	13							
slr0220	glyS	glycyl-tRNA synthetase beta chain	13	0,019				0,48		
ssr1720		similar to tyrosyl tRNA synthetase	13							
slr0922	pth	peptidyl-tRNA hydrolase	13	0,035					-0,11	
slr1673		probable tRNA/rRNA methyltransferase	13	0,008				-1,49		
slr1720	aspS	aspartyl-tRNA synthetase	13							
slr0958	cysS	cysteinyl-tRNA synthetase	13							
slr0070	fmt	methionyl-tRNA formyltransferase	13							
sll0179	gltX	glutamyl-tRNA synthetase	13							
slr1808	hemA	transfer RNA-Gln reductase	13							
slr1560	hisS	histidyl tRNA synthetase	13							
slr0357	hisS	histidyl-tRNA synthetase	13	0,028		-0,28				
sll1553	pheT	phenylalanyl-tRNA synthetase	13	0,027				0,49		
sll1425	proS	proline-tRNA ligase	13	0,044				0,63		
sll0078	thrS	threonyl-tRNA synthetase	13							

slr1884	trpS	tryptophanyl-tRNA synthetase	13							
slr1592		probable pseudouridine synthase	13							
slr0612		probable pseudouridine synthase	13							
slr0992		probable tRNA/rRNA methyltransferase	13							
sll0467		S-adenosylmethionine:tRNA ribosyltransferase-isomerase	13							
sll0844		tRNA (5-methylaminomethyl-2-thiouridylate)-methyltransferase	13							
slr0457		tRNA pseudouridine synthase B	13	0,033	-0,46					
13,2	Translation / Degradation of proteins, peptides, and glycopeptide		13							
slr0542	clpP	ATP-dependent protease ClpP	13	0,050	0,57					
sll0534	clpP2	ATP-dependent Clp protease proteolytic subunit 2	13							
slr0786		methionine aminopeptidase	13	0,017						-1,35
sll0020		ATP-dependent Clp protease ATPase subunit	13							
sll2008		processing protease	13	0.018 / 0.028		0,24			1,1	
sll0136		aminopeptidase P	13							
slr1641	clpB1	ClpB protein	13							
slr0165	clpP3	ATP-dependent Clp protease proteolytic subunit	13							
slr0008	ctpA	carboxyl-terminal processing protease	13							
sll1679	hhoA	periplasmic protease HhoA	13							
slr0021		protease	13							
slr0156	clpB2	ClpB protein	13							
slr0164	clpP4	ATP-dependent Clp protease proteolytic subunit	13							
sll0535	clpX	ATP-dependent Clp protease ATPase subunit	13	0,009				0,69		
slr0257	ctpB	periplasmic carboxyl-terminal protease	13							
slr0807		probable o-sialoglycoprotein endopeptidase	13	0.035 / 0.019	0,2				0,24	
slr1204		protease	13	0.001 / 0.023		1,44	1,08			
sll1703		protease IV	13							
slr1751		periplasmic carboxyl-terminal protease	13							
slr0659		oligopeptidase A	13							
slr1331		periplasmic processing protease	13							
sll1343		aminopeptidase	13	0.034 / 0.026		-0,76			-1,02	
sll1427		protease	13							
slr0535		protease	13							
sll0055		processing protease	13							
sll0195		probable ATP-dependent protease	13							
13,3	Translation / Nucleoproteins		13							
slr1540		mRNA-binding protein	13	0,030				-0,9		
sll1120		chromosome segregation protein SMC1	13	0,022	-0,43					
sll0517	rbp1,rbpA	putative RNA binding protein	13							
sll1712		DNA binding protein HU	13							
ssr1480	rbp2	putative RNA-binding protein	13							
slr0193	rbp3	RNA-binding protein	13							
slr1894		probable DNA-binding stress protein	13							
13,4	Translation / Protein modification and translation factors		13							
sll0830	fus	elongation factor EF-G	13	0.009 / 0.035				0,42	0,9	
slr0434	efp	elongation factor P	13							
sll0145	frr, rrf	ribosome releasing factor	13							
ssl3441	infA	initiation factor IF-1	13							
sll0227	ppiB	peptidyl-prolyl cis-trans isomerase B, periplasmic protein	13							
sll1865	prfB	peptide chain release factor 2	13							
sll1261	tsf	elongation factor TS	13							
sll0555		methionine aminopeptidase	13							
slr1251		peptidyl-prolyl cis-trans isomerase	13							
sll0546		probable translation initiation factor	13							
slr0744	infB	translation initiation factor IF-2	13							
slr0955		probable tRNA/rRNA methyltransferase	13							
slr1463	fus	elongation factor EF-G	13							
sll1099	tufA	elongation factor Tu	13	0,050				-0,57		
sll2009		processing protease	13							
sll1394		peptide methionine sulfoxide reductase	13							
sll0408		peptidyl-prolyl cis-trans isomerase	13	0,035						0,41
slr0974	infC	initiation factor IF-3	13							
slr1549		polypeptide deformylase	13							
sll0869	aat	Leu/Phe-tRNA-protein transferase	13							
sll1110	prfA	peptide chain release factor 1	13	0,026						0,18
slr1105		GTP-binding protein TypA/BipA homolog	13							
sll2001		leucine aminopeptidase	13							
slr0328		low molecular weight phosphotyrosine protein phosphatase	13							
slr0918		methionine aminopeptidase	13	0,028		0,18				
slr1795		peptide methionine sulfoxide reductase	13							
slr1228		peptide-chain-release factor 3	13							
slr1435		PmbA protein homolog	13							
slr1938		putative translation initiation factor EIF-2b subunit 1	13							
13,5	Translation / Ribosomal proteins: synthesis and modification		13							
sll1244	rpl9	50S ribosomal protein L9	13							
sll1813	rpl15	50S ribosomal protein L15	13							
slr0469	rps4	30S ribosomal protein S4	13							

sll1817	rps11	30S ribosomal protein S11	13								
sll1744	rpl1	50S ribosomal protein L1	13								
sll1802	rpl2	50S ribosomal protein L2	13								
sll1799	rpl3	50S ribosomal protein L3	13								
sll1800	rpl4	50S ribosomal protein L4	13								
sll1808	rpl5	50S ribosomal protein L5	13								
sll1810	rpl6	50S ribosomal protein L6	13								
sll1745	rpl10	50S ribosomal protein L10	13	0,035				-0,48			
sll1743	rpl11	50S ribosomal protein L11	13								
sll1746	rpl12	50S ribosomal protein L12	13								
sll1821	rpl13	50S ribosomal protein L13	13								
sll1806	rpl14	50S ribosomal protein L14	13								
sll1805	rpl16	50S ribosomal protein L16	13								
sll1819	rpl17	50S ribosomal protein L17	13	0,031				-1,15			
sll1811	rpl18	50S ribosomal protein L18	13	0.023 / 0.023				-1,07			0,5
sll1740	rpl19	50S ribosomal protein L19	13								
sll0767	rpl20	50S ribosomal protein L20	13								
sll1803	rpl22	50S ribosomal protein L22	13								
sll1801	rpl23	50S ribosomal protein L23	13	0.02 / 0.034				-0,41	0,47		
sll1807	rpl24	50S ribosomal protein L24	13								
ssr1604	rpl28	50S ribosomal protein L28	13								
ssl3436	rpl29	50S ribosomal protein L29	13								
ssr1736	rpl32	50S ribosomal protein L32	13								
ssr1398	rpl33	50S ribosomal protein L33	13								
smr0011	rpl34	50S ribosomal protein L34	13								
ssl1426	rpl35	50S ribosomal protein L35	13								
slr1356	rps1a	30S ribosomal protein S1	13								
sll1260	rps2	30S ribosomal protein S2	13								
sll1804	rps3	30S ribosomal protein S3	13								
sll1812	rps5	30S ribosomal protein S5	13	0,019					-0,6		
sll1767	rps6	30S ribosomal protein S6	13								
sll1097	rps7	30S ribosomal protein S7	13								
sll1809	rps8	30S ribosomal protein S8	13								
sll1101	rps10	30S ribosomal protein S10	13								
sll1096	rps12	30S ribosomal protein S12	13	0.023 / 0.043	0,38	-0,38					
sll1816	rps13	30S ribosomal protein S13	13	0,049					-0,62		
ssl1784	rps15	30S ribosomal protein S15	13								
ssr0482	rps16	30S ribosomal protein S16	13								
ssl3437	rps17	30S ribosomal protein S17	13								
ssr1399	rps18	30S ribosomal protein S18	13	0,033				0,82			
ssl3432	rps19	30S ribosomal protein S19	13								
slr0853		ribosomal-protein-alanine acetyltransferase	13								
ssl2233	rps20	30S ribosomal protein S20	13	0,010				0,47			
sll1967		probable RNA methyltransferase	13	0,035	0,23						
sll0754		ribosome binding factor A	13								
slr1984	nbp1,rps1l	nucleic acid-binding protein, 30S ribosomal protein S1 homolog	13								
sll1824	rpl25	50S ribosomal protein L25	13	0.027 / 0.007				1,27			-0,17
slr0361		probable ribosomal large subunit pseudouridine synthase B	13								
slr1678	rpl21	50S ribosomal protein L21	13								
ssr2799	rpl27	50S ribosomal protein L27	13								
slr0628	rps14	30S ribosomal protein S14	13								
ssl3445	rpl31	50S ribosomal protein L31	13								
sml0006	rpl36	50S ribosomal protein L36	13								
sll1822	rps9	30S ribosomal protein S9	13								
ssl0601	rps21	30S ribosomal protein S21	13					1,1			
slr0808		16S rRNA processing protein RimM homolog	13								
sll0825		polyA polymerase	13								
sll1909		probable methyltransferase	13								
slr1629		ribosomal large subunit pseudouridine synthase D	13								
ssl0438		similar to 50S ribosomal protein L12	13								
14,1	Transport and binding proteins / C		14								
sll0771	glcP, gtr	glucose transport protein	14								
slr0044	cmpD	bicarbonate transport system ATP-binding protein	14								
slr1224		ATP-binding protein of sugar ABC transporter	14								
slr0040	cmpA	bicarbonate transport system substrate-binding protein	14								
slr0041	cmpB	bicarbonate transport system permease protein	14	0,015					-0,83		
slr0043	cmpC	bicarbonate transport system ATP-binding protein	14	0.034 / 0.049 / 0.035	0,78			-1,34			0,8
slr1897		periplasmic sugar-binding protein of ABC transporter	14								
slr1723		permease protein of sugar ABC transporter	14								
slr1202		permease protein of sugar ABC transporter	14								
14. 8	Transport and binding proteins / Osmoregulation		14								
slr2057		water channel protein	14								
slr0747	ggtA	glucosylglycerol transport system ATP-binding protein	14								
slr0529	ggtB	glucosylglycerol transport system substrate-binding protein	14								

slr0530	ggtC	glucosylglycerol transport system permease protein	14								
slr0531	ggtD	glucosylglycerol transport system permease protein	14	0.036 / 0.044				-0,6	-0,25		
slr0875		large-conductance mechanosensitive channel	14								
slr0639		mechanosensitive ion channel homolog	14								
14,2	Transport and binding proteins / N		14								
sll1452	nrtC	nitrate/nitrite transport system ATP-binding protein	14								
sll1453	nrtD	nitrate/nitrite transport system ATP-binding protein	14								
sll1017	amt2	ammonium/methylammonium permease	14								
sll0537	amt3	ammonium/methylammonium permease	14								
slr0447	urtA	periplasmic protein, ABC-type urea transport system substrate-binding protein	14								
sll0764	urtD	urea transport system ATP-binding protein	14								
sll0374	urtE	urea transport system ATP-binding protein	14								
slr1201		urea transport system permease protein	14								
slr1200		urea transport system permease protein	14								
sll1450	nrtA	nitrate/nitrite transport system substrate-binding protein	14								
sll1451	nrtB	nitrate/nitrite transport system permease protein	14								
sll0108	amt1	ammonium/methylammonium permease	14								
14,3	Transport and binding proteins / Amino acids		14								
sll0146	natC	Integral membrane protein of the ABC-type, Nat permease for neutral amino acids	14								
slr1735	bgtA	ATP-binding subunit of the ABC-type Bgt permease for basic amino acids and glutamine	14								
slr0559	natB	periplasmic binding protein of ABC transporter for natural amino acids	14	0,044							-0,1
sll0224		amino-acid ABC transporter binding protein	14	0,001							1,09
sll1762		periplasmic protein, putative polar amino acid transport system substrate-binding protein	14								
sll1270	bgtB	periplasmic substrate-binding and integral membrane protein of the ABC-type Bgt permease for basic amino acids and glutamine BgtB	14								
sll1102	gtrA	integral membrane protein (small) of a TRAP-type permease that mediates sodium-dependent glutamate transport GtrA	14								
sll1103	gtrB	integral membrane protein (large) of a TRAP-type permease that mediates sodium-dependent glutamate transport GtrB	14								
sll1104	gtrC	periplasmic substrate-binding protein of a TRAP-type permease that mediates sodium-dependent glutamate transport GtrC	14								
slr1145	gltS	Monocomponent sodium-dependent glutamate permease GltS	14								
slr0467	natA	conserved component of ABC transporter for natural amino acids	14								
slr0949	natD	Integral membrane protein of the ABC-type Nat permease for neutral amino acids NatD	14								
slr1881	natE	ATP-binding subunit of the ABC-type Nat permease for neutral amino acids	14	0,002					-0,43		
slr0401		periplasmic polyamine-binding protein of ABC transporter	14								
sll0064		periplasmic protein, putative polar amino acid transport system substrate-binding protein	14								
14,4	Transport and binding proteins /Fe		14								
slr1890		bacterioferritin	14								
sll1341		bacterioferritin	14								
slr0242		bacterioferritin comigratory protein homolog	14								
slr1392	feoB	ferrous iron transport protein B	14								
slr1295	futA1	iron transport system substrate-binding protein	14								
slr0513		iron transport system substrate-binding protein, periplasmic protein	14	0,009							1,26
slr1318		iron(III) dicitrate transport system ATP-binding protein	14	0,008							0,94
sll1878		iron(III)-transport ATP-binding protein	14								
slr0327		iron(III) ABC transporter, permease protein	14								
slr1492		iron(III) dicitrate transport system substrate-binding protein	14								
slr1490		ferrichrome-iron receptor	14								
sll1202		iron(III) dicitrate-binding protein of ABC transporter, FecB homolog	14								
sll1406		ferrichrome-iron receptor	14								
sll1409		ferrichrome-iron receptor	14	0,049							0,17
slr1319		iron(III) dicitrate transport system substrate-binding protein	14	0.044 / 0.032				-0,08	0,6		
sll0221		bacterioferritin comigratory protein	14								
sll1206		ferric aerobactin receptor, FhuA homolog	14								
slr1317		ABC-type iron(III) dicitrate transport system permease protein	14								
slr1316		ABC-type iron(III) dicitrate transport system permease protein	14								

slr1491		iron(III) dicitrate transport system substrate-binding protein	14							
14,5	Transport and binding proteins / Other cations		14							
sll0738		molybdate-binding periplasmic protein	14							
sll1598	mntC	manganese transporter MntC	14	0.047 / 0.002			1,25			2,44
slr2043		zinc transport system substrate-binding protein	14							
slr0797	coaT	cobalt-transporting P-type ATPase (cobalt efflux pump) involved in cobalt tolerance	14	0,005				1,12		
sll1263		cation efflux system protein	14							
slr0822		cation-transporting P-type ATPase PacL	14							
sll1076	pacL	cation-transporting ATPase PacL	14							
sll1614	pma1	cation-transporting P-type ATPase	14							
sll0672	pacL	cation-transporting p-type ATPase PacL	14							
slr1950	ctaA	copper-transporting P-type ATPase CtaA	14							
sll1920	pacS	copper-transporting P-type ATPase PacS	14							
slr1457		chromate transport protein	14	0,009						-0,35
slr0014		Mg2+ transport ATPase	14							
slr1216		Mg2+ transport protein	14							
sll1599	mntA	manganese transport system ATP-binding protein MntA	14							
sll1600	mntB	manganese transport system membrane protein MntB	14							
sll0739		ATP-binding protein of molybdate ABC transporter	14	0,009						-0,34
ssr2857	atx1	mercuric transport protein periplasmic component precursor	14							
slr0796	nrsD	nickel permease involved in nickel and cobalt tolerance	14							
slr0794	nrsA	cation efflux system protein involved in nickel and cobalt tolerance	14							
slr0798	ziaA	zinc-transporting P-type ATPase (zinc efflux pump) involved in zinc tolerance	14							
slr2044		zinc transport system ATP-binding protein	14	0,005						0,92
slr2045		zinc transport system permease protein	14							
14,6	Transport and binding proteins / H, Na, K, Ca		14							
slr1509	ktrB, ntpJ	membrane subunit of a Ktr-like ion transport system	14	0,012	0,19					
slr1728	kdpA	potassium-transporting P-type ATPase A chain	14							
slr1731	kdpD	potassium-transporting P-type ATPase D chain	14							
sll0993		potassium channel	14	0,042	0,46					
sll0689	nhaS3	Na+/H+ antiporter	14							
slr1729	kdpB	potassium-transporting P-type ATPase B chain	14							
slr1730	kdpC	potassium-transporting P-type ATPase C chain	14							
sll0273	nhaS2	Na+/H+ antiporter	14							
slr1595	nhaS4	Na+/H+ antiporter	14							
slr0415	nhaS5	Na+/H+ antiporter	14							
slr1727		Na+/H+ antiporter	14	0.037 / 0.031		-0,69			-1,12	
sll0556		Na+/H+ antiporter	14							
slr1336		H+/Ca2+ exchanger	14							
slr1596	pxcA	a protein in the cytoplasmic membrane involved in light-induced proton extrusion.	14							
14,6	Transport and binding proteins / P		14							
sll0679		periplasmic phosphate-binding protein of ABC transporter	14							
sll0683		phosphate transport ATP-binding protein PstB homolog	14							
sll0684		phosphate transport ATP-binding protein PstB homolog	14							
slr1250		phosphate transport ATP-binding protein PstB homolog	14							
sll0682		phosphate transport system permease protein PstA homolog	14							
slr1249		phosphate transport system permease protein PstA homolog	14	0,036		0,42				
sll0681		phosphate transport system permease protein PstC homolog	14							
slr1248		phosphate transport system permease protein PstC homolog	14	0,020	0,42					
sll0680		phosphate-binding periplasmic protein precursor (PBP)	14							
slr1247		phosphate-binding periplasmic protein precursor (PBP)	14							
sll0540		phosphate-binding protein PstS homolog	14							
14,7	Transport and binding proteins / S		14							
slr0096		low affinity sulfate transporter	14							
slr1455	cysA	sulfate transport system ATP-binding protein	14							
slr1452	sbpA	sulfate transport system substrate-binding protein	14							
sll1041	cysA	similar to sulfate transport ATP-binding protein CysA	14	0.038 / 0.038	-0,44	-0,3				
slr1453	cysT	sulfate transport system permease protein	14							
slr1454	cysW	sulfate transport system permease protein	14							
slr1776		high affinity sulfate transporter	14							

sll0834		low affinity sulfate transporter	14							
slr1229		sulfate permease	14	0,008					-0,96	
14,9	Transport and binding proteins/ ABC transporters		14							
slr0615		ATP-binding protein of ABC transporter	14	0,014					0,73	
slr0251	ycf85	ATP-binding protein of ABC transporter	14							
slr1901		ATP-binding protein of ABC transporter	14							
sll1082		ABC transport system ATP-binding protein	14							
sll1623		ABC transporter ATP-binding protein	14							
sll1481		ABC-transporter membrane fusion protein	14	0,009					0,34	
slr1113		ATP-binding protein of ABC transporter	14							
sll1001		ATP-binding protein of ABC transporter	14							
sll1870		ATP-binding protein of ABC transporter	14							
sll1081		ABC transport system permease protein	14							
slr0544		ATP-binding protein of ABC transporter	14	0,017				-0,29		
sll0489		ATP-binding protein of ABC transporter	14							
sll0484		ATP-binding protein of ABC transporter	14							
slr1651		ABC transporter ATP-binding protein	14							
slr0977		ABC transporter, permease component	14							
slr0075	ycf16	ABC transporter ATP-binding protein	14							
slr0074	ycf24	ABC transporter subunit	14							
sll0912		ABC transporter ATP binding protein	14							
sll1927		ABC transporter ATP-binding protein	14							
sll0240		ABC transporter ATP-binding protein	14							
sll0182		ABC transporter ATP-binding protein	14							
sll0759		ABC transporter ATP-binding protein	14							
sll1482		ABC transporter permease protein	14							
sll0778		ABC transporter, ATP-binding protein	14							
slr2019		ATP-binding protein of ABC transporter	14							
sll0385		ATP-binding protein of ABC transporter	14	0,022						-1,49
sll1725		ATP-binding protein of ABC transporter	14							
slr0354		ATP-binding protein of ABC transporter	14	0.048 / 0.02	-0,39					-0,47
sll1276		ATP-binding protein of ABC transporter	14							
slr1149		ATP-binding protein of ABC transporter	14	0,020				-1,6		
sll0415		ATP-binding protein of ABC transporter	14							
slr0864		ATP-binding protein of ABC transporter	14							
14.10	Transport and binding proteins / Secretion		14							
sll1404		biopolymer transport ExbB protein homolog	14							
sll1405		biopolymer transport ExbD protein homolog	14							
slr0677		biopolymer transport ExbB like protein	14							
slr1488		multidrug resistance family ABC transporter	14							
slr1740		oligopeptide binding protein of ABC transporter	14	0,027						0,7
sll1699		oligopeptide-binding protein of oligopeptide ABC transporter	14							
slr0678		biopolymer transport ExbD like protein	14							
sll1180		toxin secretion ABC transporter ATP-binding protein	14							
slr1494		MDR (multidrug resistance) family ABC transporter	14							
slr0896		multi-drug efflux transporter	14							
slr0944		multidrug-efflux transporter	14							
slr0454		RND multidrug efflux transporter	14							
slr0369		RND multidrug efflux transporter	14							
slr2131		RND multidrug efflux transporter	14	0,010				-0,69		
14.11	Transport and binding proteins / Other		14							
sll0895		CysQ protein homolog	14							
slr0817	menF	salicylate biosynthesis isochorismate synthase	14							
14.12	Transport and binding proteins / Suggested annotation		14							
sll0574		probable permease protein of lipopolysaccharide ABC transporter	14							
slr0681		probable sodium/calcium exchanger protein	14							
sll1428		probable sodium-dependent transporter	14	0,042				-0,58		
sll0477		putative biopolymer transport ExbB-like protein	14							
sll0536		probable potassium channel protein	14							
sll1374		probable sugar transporter	14	0,022					0,57	
sll1087		similar to sodium/glucose cotransporter	14	0,035						0,99
sll0507		probable cation transporter	14							
sll0575		probable lipopolysaccharide ABC transporter ATP binding subunit	14							
slr2108		probable polysaccharide ABC transporter ATP binding subunit	14							
slr1575		probable potassium efflux system	14	0,032						0,38
slr0753		probable transport protein	14	0.043 / 0.04					0,6	1,02
ssl3127		similar to permease protein of ABC transporter	14							
slr2077		probable ABC transporter, periplasmic binding protein	14							
slr1794		probable anion transporting ATPase	14							
sll0142		probable cation efflux system protein	14							
sll0671		probable cation transporter	14							
sll1864		probable chloride channel protein	14							
sll0312		probable oligopeptides ABC transporter permease protein	14							

slr0324		probable oligopeptides ABC transporter permease protein	14	0,002					-0,7	
sll0833		probable oligopeptides ABC transporter permease protein	14							
sll1768		probable oligopeptides ABC transporter permease protein	14							
slr0347		probable permease protein of ABC transporter	14							
slr0982		probable polysaccharide ABC transporter ATP binding subunit	14	0,008						-0,83
slr2107		probable polysaccharide ABC transporter permease protein	14							
sll0640		probable sodium/sulfate symporter	14							
sll0855		putative channel transporter	14							
sll1204		similar to macrolide efflux protein	14	0,033						0,52
15,1	Other categories / Adaptations and atypical conditions		15							
sll1968	pmgA	photomixotrophic growth related protein, PmgA	15							
slr1246		putative transposase [ISY802_b]	15							
sll1983		putative transposase [ISY100_n]	15							
slr2112		putative transposase [ISY100_o]	15							
sll1677		similar to spore maturation protein B	15							
slr1106		prohibitin	15	0,029						0,79
sll0698	dspA, dfr,	drug sensory protein A, low temperature sensor, two-component sensor histidine kinase	15							
sll1462	hypE	putative hydrogenase expression/formation protein HypE	15							
slr1521		GTP-binding protein	15							
sll1556		isopentenyl-dephosphate delta-isomerase	15							
sll0829		probable methyltransferase	15	0,029						0,09
sll1154		putative antibiotic efflux protein	15							
15,2	Other categories / Drug and analog sensitivity		15							
sll0947	lrtA	light repressed protein A homolog	15	0,039					1,35	
sll1308		probable oxidoreductase	15	0,040						0,61
slr2135	hupE	hydrogenase accessory protein HupE	15							
slr2002	cphA	cyanophycin synthetase	15							
sll1397		putative transposase [ISY100_a]	15							
ssr2899		putative transposase	15							
sll1513	ccsA, ycf5	c-type cytochrome synthesis protein	15							
slr1523		putative transposase	15	0,046						-0,51
slr1409		periplasmic WD-repeat protein	15							
slr0143	hat	WD-repeat protein, Hat protein, involved in the control of a high-affinity transport system for inorganic carbon	15	0,008	0,32					
slr0697		5-oxoprolinase homolog	15	0,001						-0,4
sll0708		dimethyladenosine transferase	15							
sll1284		esterase	15							
slr1019		phenazine biosynthetic protein PhzF homolog	15	0,042				-1,17		
slr1077		plobable glycosyltransferase	15							
sll0644		probable esterase	15	0,049				-1,3		
sll1647		probable phosphinothricin N-acetyltransferase	15							
sll0777		putative carboxypeptidase	15							
slr0782		putative flavin-containing monoamine oxidase	15	0,035						0,19
sml0010		putative transposase	15							
sll1984		putative transposase [ISY100_n]	15							
sll1474		putative transposase [ISY203_g]	15							
sll0092		putative transposase [ISY391_c]	15							
15,3	Other categories / Hydrogenase		15							
slr0067		MRP protein homolog	15	0,013						0,67
sll1559		soluble hydrogenase 42 kD subunit	15							
sll1432	hypB	putative hydrogenase expression/formation protein HypB	15							
slr2096		putative transposase [ISY120_c]	15	0,034						-0,56
slr0379		thymidylate kinase	15							
slr0857		putative transposase [ISY100_l]	15							
slr0099		putative transposase [ISY352_f]	15							
slr1675	hypA1	putative hydrogenase expression/formation protein HypA1	15							
sll0506		undecaprenyl pyrophosphate synthetase	15							
sll1910	zam	protein conferring resistance to acetazolamide Zam	15							
slr1140		DegT/DnrJ/EryC1/StrS family protein	15							
slr1076		plobable glycosyltransferase	15							
sll1869		probable dioxygenase, Rieske iron-sulfur component	15	0,027				0,09		
slr0180		putative transposase [ISY203_f]	15							
sll0163		WD-repeat protein	15	0,042						-0,7
15,4	Other categories / Other (with gene code and annotation)		15							
sll1032	ccmN	carbon dioxide concentrating mechanism protein CcmN, putative carboxysome assembly protein	15							
slr2087	ccs1, ycf44	c-type cytochrome biogenesis protein Ccs1	15	0,044						0,15
slr2094	fbpI	fructose-1,6-/sedoheptulose-1,7-bisphosphatase	15	0.038 / 0.013		0,14			-0,29	
slr1942	kaiC3	circadian clock protein KaiC homolog	15							

ssr1789	hliD, scpE	CAB/ELIP/HLIP-related protein HliD	15							
slr0116	pcyA	phycocyanobilin:ferredoxin oxidoreductase	15							
sll1786	tatD	putative deoxyribonuclease, tatD homolog	15							
ssl2542	hliA, scpC	high light-inducible polypeptide HliA, CAB/ELIP/HLIP superfamily	15							
ssr2595	hliB, scpD	high light-inducible polypeptide HliB, CAB/ELIP/HLIP superfamily	15							
slr1498	hypD	putative hydrogenase expression/formation protein HypD	15							
sll1221	hoxF	diaphorase subunit of the bidirectional hydrogenase	15							
sll1079	hypB	putative hydrogenase expression/formation protein HypB	15							
sll1596	kaiB2	circadian clock protein KaiB homolog	15							
sll1595	kaiC2	circadian clock protein KaiC homolog	15							
slr0756	kaiA	circadian clock protein KaiA homolog	15							
slr1302	cupB	protein involved in constitutive low affinity CO2 uptake	15	0,006			-0,34			
slr2097	glbN	cyanoglobin	15							
sll1220	hoxE	putative diaphorase subunit of the bidirectional hydrogenase	15							
sll1226	hoxH	hydrogenase subunit of the bidirectional hydrogenase	15							
sll1223	hoxU	diaphorase subunit of the bidirectional hydrogenase	15	0.034 / 0.047		-0,38			0,31	
sll1078	hypA2	putative hydrogenase expression/formation protein HypA	15							
sll1900	act	acetyltransferase	15	0,019	-0,47					
slr0946	arsC	arsenate reductase	15	0.029 / 0.027	0,47			-0,48		
sll0621	ccdA	putative c-type cytochrome biogenesis protein CcdA	15							
slr2001	cphB	cyanophycinase	15							
sll1489	cpmA	circadian phase modifier CpmA homolog	15							
sll1224	hoxY	hydrogenase subunit of the bidirectional hydrogenase	15	0,010				-0,63		
ssl3580	hypC	putative hydrogenase expression/formation protein HypC	15	0,024						-0,93
sll0322	hypF	putative hydrogenase expression/formation protein HypF	15							
slr0758	kaiC1	circadian clock protein KaiC homolog	15	0,033						0,49
slr0757	kaiB1	circadian clock protein KaiB homolog	15							
sll0486	kaiB3	circadian clock protein KaiB homolog	15							
sll1653	menG	2-phytyl-1,4-benzoquinone methyltransferase	15							
slr0746	stpA	glucosylglycerolphosphate phosphatase	15							
15.4.2	Other categories / Other (with annotation only)		15							
sll0019		1-deoxy-d-xylulose 5-phosphate reductoisomerase	15	0,008					-1,09	
ssl2250		bacterioferritin-associated ferredoxin	15							
slr1853		carboxymuconolactone decarboxylase	15	0,014						-0,65
slr1761		FKBP-type peptidyl-prolyl cis-trans isomerase, periplasmic protein	15							
slr2136		GcpE protein homolog	15							
sll0480		probable aminotransferase	15							
sll1305		probable hydrolase	15							
slr1763		probable methyltransferase	15	0,017					-1,34	
slr2053		putative hydrolase	15							
sll1300		putative methyltransferase	15							
sll0222		putative purple acid phosphatase	15							
sll0654		alkaline phosphatase	15							
slr1974		GTP binding protein	15							
sll1534		probable glycosyltransferase	15							
sll1033		probable protein phosphatase	15							
slr2123		similar to D-3-phosphoglycerate dehydrogenase	15							
sll1621		AhpC/TSA family protein	15							
slr1198		antioxidant protein	15							
slr0095		O-methyltransferase	15							
sll0002		penicillin-binding protein	15							
slr1085		plobable glycosyltransferase	15	0,006						-0,87
slr1610		putative C-3 methyl transferase	15							
slr0703		putative transposase [ISY523_i]	15							
slr0799		putative transposase [ISY802_c]	15							
slr0381		lactoylglutathione lyase	15							
sll1434		penicillin-binding protein	15							
slr1075		putative transposase [ISY100_b]	15							
slr0352		putative transposase [ISY100_e]	15							
sll0699		putative transposase [ISY100_i]	15							
sll0650		putative transposase [ISY100_j]	15							
sll0651		putative transposase [ISY100_j]	15							
sll1256		putative transposase [ISY100_p]	15							
slr1522		putative transposase [ISY352_d]	15							
sll0808		putative transposase [ISY508_a]	15							
slr1585		putative transposase [ISY508_c]	15	0,001		-0,63				

sll0818		tetrapyrrole methylase family protein	15								
sll0219		flavoprotein	15								
sll1297		probable dioxygenase, Rieske iron-sulfur component	15								
sll0501		probable glycosyltransferase	15								
slr1748		probable phosphoglycerate mutase	15	0,026	0,16						
sll0034		putative carboxypeptidase	15								
ssl3649		putative transposase	15								
ssl1507		putative transposase [ISY508_a]	15								
sll1710		putative transposase [ISY523_b]	15								
slr0265		putative transposase [ISY523_c]	15								
slr0511		putative transposase [ISY523_g]	15								
ssr2699		putative transposase [ISY523_k]	15								
ssr2898		putative transposase [ISY523_m]	15								
sll1861		putative transposase [ISY523_o]	15								
ssl0296		putative transposase [ISY523_p]	15								
sll0665		putative transposase [ISY523_r]	15								
sll1792		putative transposase [ISY802_a]	15								
slr1626		dihydroneopterin aldolase	15	0,038					0,94		
slr1065		plobable glycosyltransferase	15								
slr0862		probable sugar kinase	15								
sll0550		flavoprotein	15								
sll1664		probable glycosyl transferase	15								
sll1407		probable methyltransferase	15								
sll0700		putative transposase [ISY100_i]	15								
sll1791		putative transposase [ISY802_a]	15								
sll1129		2-hydroxy-6-oxohepta-2,4-dienoate hydrolase	15								
slr0319		beta-lactamase	15								
sll0873		carboxynorspermidine decarboxylase	15								
slr0201		heterodisulfide reductase subunit B	15								
slr0314		non-heme chloroperoxidase	15								
sll0915		periplasmic protease	15								
slr1410		periplasmic WD-repeat protein	15								
slr2047		PhoH like protein	15								
sll1020		plobable glycosyltransferase	15								
slr1501		probable acetyltransferase	15	0,013						1,66	
slr1192		probable alcohol dehydrogenase	15	0,032							5,06
slr0700		probable amino acid permease	15								
sll0264		probable dioxygenase Rieske iron-sulfur component	15	0,028		0,26					
slr0231		probable DNA-3-methyladenine glycosylase	15								
slr1508		probable glycosyltransferase	15								
sll1466		probable glycosyltransferase	15								
slr2126		probable glycosyltransferase	15								
slr0626		probable glycosyltransferase	15								
sll1723		probable glycosyltransferase	15								
sll0245		probable GTP binding protein	15								
slr1772		probable hydrolase, periplasmic protein	15								
slr0309		probable methyltransferase	15	0,033							-0,83
sll0816		probable oxidoreductase	15	0,013						-0,57	
slr0825		probable peptidase	15								
slr1420		probable sugar kinase	15								
slr0007		probable sugar-phosphate nucleotidyltransferase	15								
sll0135		putative 5'-methylthioadenosine phosphorylase	15								
sll1848		putative acyltransferas	15								
sll0086		putative arsenical pump-driving ATPase	15								
sll1298		putative carboxymethylenebutenolidase	15								
sll0992		putative esterase	15	0,008		-0,11					
ssr2227		putative transposase	15								
smr0012		putative transposase	15								
slr1496		putative transposase	15								
ssl0769		putative transposase	15	0,029							-0,5
sll1094		putative transposase	15								
ssl1277		putative transposase	15								
slr1357		putative transposase [ISY100_c]	15								
sll1998		putative transposase [ISY100_d]	15								
slr0230		putative transposase [ISY100_f]	15								
slr0704		putative transposase [ISY100_g]	15								
sll0431		putative transposase [ISY100_h]	15								
slr2113		putative transposase [ISY100_o]	15								
sll0201		putative transposase [ISY100_s]	15								
ssl0426		putative transposase [ISY100_t]	15								
sll1255		putative transposase [ISY203_c]	15								
ssr3452		putative transposase [ISY352_a]	15								
slr1683		putative transposase [ISY391_b2]	15	0,030	-0,69						
slr0378		similar to 7-beta-(4-carbaxybutanamido)cephalosporanic acid acylase	15								
slr0788		similar to pre-B cell enhancing factor	15								
slr1197		SMF protein	15								
sll1459		stationary-phase survival protein SurE homolog	15								

15,5	Other categories / Transposon-related functions	15							
sll1945	1-deoxyxylulose-5-phosphate synthase	15							
sll0648	probable glycosyltransferase	15	0,044				-0,48		
sll0576	putative sugar-nucleotide epimerase/dehydratease	15	0,006						0,73
slr1205	similar to chlorobenzene dioxygenase, ferredoxin component	15							
sll1108	stationary-phase survival protein SurE homolog	15	0,029					-0,97	
slr0665	aconitate hydratase	15	0,004				0,23		
slr1903	putative transposase [ISY120_a]	15	0,009						-0,67
slr1902	putative transposase [ISY120_a]	15							
sll1157	putative transposase [ISY120_b]	15	0,028						-0,53
sll1156	putative transposase [ISY120_b]	15	0,021						-0,39
slr2095	putative transposase [ISY120_c]	15							
sll0986	putative transposase [ISY120_f]	15	0,048						-0,57
slr0460	putative transposase [ISY352_g1]	15							
sll0677	putative transposase [ISY523_h]	15							
ssl1920	putative transposase [ISY523_l]	15							
slr1960	putative transposase	15							
slr0856	putative transposase [ISY100_l]	15							
slr1715	putative transposase [ISY100_m]	15							
sll1436	putative transposase [ISY100_q]	15							
slr1936	putative transposase [ISY100_r]	15							
sll0200	putative transposase [ISY100_s]	15							
slr1524	putative transposase [ISY100_u]	15							
ssr1175	putative transposase [ISY100_v1]	15							
sll1982	putative transposase [ISY352_c2]	15							
sll0667	putative transposase [ISY352_e2]	15							
slr1282	putative transposase [ISY508_b]	15							
sll0217	flavoprotein	15							
sll1159	probable bacterioferritin comigratory protein	15							
sll1849	probable dioxygenase Rieske iron-sulfur component	15							
sll1704	probable short chain dehydrogenase	15							
slr0078	putative 6-pyruvoyl tetrahydrobiopterin synthase	15							
sll1369	putative peptidase	15							
ssr1176	putative transposase [ISY100_v3]	15							
slr1283	putative transposase [ISY508_b]	15							
sll1716	putative transposase [ISY523_a]	15	0,010			-0,2			
sll1860	putative transposase [ISY523_d]	15							
slr0350	putative transposase [ISY523_e]	15							
sll0012	putative transposase [ISY523_f]	15							
ssl1922	putative transposase [ISY523_l]	15	0,011			-0,4			
ssr0256	putative transposase [ISY523_n]	15							
slr0166	putative transposase [ISY523_n]	15							
sll0666	putative transposase [ISY523_r]	15							
sll0161	putative transposase [ISY524_p]	15							
slr0800	putative transposase [ISY802_c]	15							
slr0880	similar to fibronectin binding protein	15							
slr1063	plobable glycosyltransferase	15	0,032						-0,82
sll0936	putative oxidoreductase	15							
slr2062	putative transposase [ISY052_a]	15	0,031						0,34
slr1764	similar to tellurium resistance protein TerE	15							
sll1971	probable hexosyltransferase	15							
sll1930	putative transposase [ISY100_k]	15							
slr1635	putative transposase [ISY203_e]	15							
ssr2078	putative transposase [ISY802_b]	15							
ssr1169	stress induced hydrophobic peptide homolog	15	0,009				1,17		
slr1542	2-C-methyl-D-erythritol 2,4-cyclodiphosphate synthase	15							
slr1556	2-hydroxyacid dehydrogenase homolog	15							
slr0951	4-diphosphocytidyl-2C-methyl-D-erythritol synthase	15							
slr1888	4-hydroxybutyrate coenzyme A transferase.	15	0,012						-0,52
slr0580	aluminum resistance protein homolog	15	0,037					1,07	
slr0945	arsenical resistance protein ArsH homolog	15							
sll0210	bacitracin resistance protein	15	0.037 / 0.011	0,35			0,36		
slr1719	DrgA protein homolog	15	0,007				-1,03		
sll1636	ferripyochelin binding protein	15							
sll1521	flavoprotein	15							
slr0298	FraH protein homolog	15							
sll0990	glutathione-dependent formaldehyde dehydrogenase	15							
slr0604	GTP-binding protein	15							
slr0245	Histone deacetylase family protein	15							
sll0711	isopentenyl monophosphate kinase	15	0,045						
slr1520	oxidoreductase, aldo/keto reductase family	15							
sll1833	penicillin-binding protein	15							
slr1710	penicillin-binding protein	15							
sll1491	periplasmic WD-repeat protein	15							
sll0395	phosphoglycerate mutase	15	0,011				-0,5		
slr0541	probable amidotransferase	15	0,003						-0,51

sll0686		probable cytochrome c-type biogenesis protein	15	0,038						-1,27
slr1916		probable esterase	15	0,012					0,72	
sll1377		probable glycosyltransferase	15							
slr1849		probable mercuric reductase	15							
slr1115		probable methyltransferase	15							
slr1208		probable oxidoreductase	15							
slr0315		probable oxidoreductase	15							
slr0537		putative sugar kinase	15	0,004						0,75
slr1716		putative transposase [ISY100_m]	15							
sll1257		putative transposase [ISY100_p]	15							
sll1437		putative transposase [ISY100_q]	15							
smr0002		putative transposase [ISY100_v2]	15							
slr1937		putative transposase [ISY101_r]	15							
slr2036		putative transposase [ISY203_a]	15							
sll1780		putative transposase [ISY203_b]	15							
sll1560		putative transposase [ISY203_d]	15							
sll1999		putative transposase [ISY203_h1]	15							
sll1997		putative transposase [ISY203_h2]	15							
sll0317		putative transposase [ISY203_i1]	15							
sll0315		putative transposase [ISY203_i2]	15							
sll1985		putative transposase [ISY352_c1]	15							
ssr0871		putative transposase [ISY352_e1]	15							
sll0668		putative transposase [ISY352_e2]	15	0,001				1,13		
ssr0817		putative transposase [ISY352_g2]	15							
slr0462		putative transposase [ISY352_g2]	15							
slr1682		putative transposase [ISY391_b1]	15							
slr1684		putative transposase [ISY391_b2]	15							
ssl0172		putative transposase [ISY391_c]	15	0,048						0,61
slr1586		putative transposase [ISY508_c]	15							
slr1109		similar to ankyrin	15	0,036						-0,5
sll1253		similar to polyA polymerase	15							
sll1678		similar to spore maturation protein A	15							
sll1283		similar to stage II sporulation protein D	15							
slr1639		SsrA-binding protein	15							
slr0679		sun protein	15	0,026					0,69	
15,6	Other categories / WD repeat proteins		15							
sll1959		probable inositol monophosphatase	15							
sll0626		putative neutral invertase	15							
slr0338		probable oxidoreductase	15							
sll1758		MrsA protein homolog	15	0,017						0,51
ssl2789		similar to resolvase	15	0,036		-0,39				
16,1	Hypothetical / with gene code and suggested annotation		16							
ssl1911	gifA	glutamine synthetase inactivating factor IF7	16							
sll1281	psbZ, ycf9	photosystem II PsbZ protein	16	0,021		-0,51				
slr1780	ycf54	hypothetical protein YCF54	16							
sll1737	ycf60	hypothetical protein YCF60	16							
slr0011	rbcX	possible Rubisco chaperonin	16							
sll0558	ycf53	hypothetical protein YCF53	16							
sll1214	ycf59	hypothetical protein YCF59	16							
slr0923	ycf65	hypothetical protein YCF65	16							
ssl3364	cp12	CP12 polypeptide	16							
ssl1633	hliC, scpB	high light-inducible polypeptide HliC, CAB/ELIP/HLIP superfamily	16							
sll1797	ycf21	hypothetical protein YCF21	16							
ssr1425	ycf34	hypothetical protein YCF34	16							
sll0760	ycf38	hypothetical protein YCF38	16							
slr0480	ycf46	hypothetical protein YCF46	16							
slr0197	comA	competence protein	16							
ssr2142	ycf19	hypothetical protein YCF19	16							
ssl1417	ycf33	hypothetical protein YCF33	16							
sll0608	ycf49	hypothetical protein YCF49	16	0,014					0,33	
slr0503	ycf66	hypothetical protein YCF66	16							
slr2032	ycf23	hypothetical protein YCF23	16							
sll0661	ycf35	hypothetical protein YCF35	16							
sll0617	vipp1	plasma membrane protein essential for thylakoid formation	16	0,045						-0,28
sll0047	ycf12	hypothetical protein YCF12	16							
sll1218	ycf39	hypothetical protein YCF39	16							
slr1034	ycf41	hypothetical protein YCF41	16	0,044					0,2	
slr1045	ycf63	hypothetical protein YCF63	16							
slr0882	ycf84	hypothetical protein YCF84	16							
sll0821	cph2	phytochrome-like protein	16							
sll0033	crtH	carotene isomerase	16							
sll1734	cupA	protein involved in low CO2-inducible, high affinity CO2 uptake	16							
slr1515	ictB	putative membrane protein required for bicarbonate uptake	16							
slr0795	nrsC	cation efflux system protein involved in nickel and cobalt tolerance	16	0,036						-0,62

slr2031	rsbU	putative PP2C-type protein phosphatase, gene required to recover from the nitrogen or sulfate starvation induced stationary phase	16								
slr1512	sbtA	sodium-dependent bicarbonate transporter	16								
sll0173	vgb	virginiamycin B hydrolase, periplasmic protein	16	0,021					-0,82		
sll1509	ycf20	hypothetical protein YCF20	16								
sll0751	ycf22	hypothetical protein YCF22	16	0,044							0,46
sll1002	ycf22	hypothetical protein YCF22	16								
sll0584	ycf36	hypothetical protein YCF36	16								
slr0399	ycf39	chaperon-like protein for quinone binding in photosystem II	16	0,015							0,58
slr1218	ycf39	hypothetical protein YCF39	16								
ssr0102	ycf40	hypothetical protein YCF40	16								
slr0692	ycf45	hypothetical protein YCF45	16	0,037							-0,64
slr2073	ycf50	hypothetical protein YCF50	16								
sll1702	ycf51	hypothetical protein YCF51	16								
sll0286	ycf52	hypothetical protein YCF52	16								
slr0050	ycf56	hypothetical protein YCF56	16	0,048					-0,95		
slr1417	ycf57	hypothetical protein YCF57	16	0,018		0,42					
slr2049	ycf58	hypothetical protein YCF58	16								
ssl2982	ycf61	probable DNA-directed RNA polymerase omega subunit	16								
slr1278	ycf62	hypothetical protein YCF62	16								
slr1972	ycf81	hypothetical protein YCF81	16								
slr0204	ycf83	hypothetical protein YCF83	16								
16,2	Hypothetical / without gene code but with suggested annotation		16								
slr1963		water-soluble carotenoid protein	16								
sll1080		ABC transport system substrate-binding protein	16								
sll1549		salt-enhanced periplasmic protein	16								
slr1608		putative glucose dehydrogenase-B, periplasmic protein	16								
sll1358		putative oxalate decarboxylase, periplasmic protein	16								
sll0662		4Fe-4S type iron-sulfur protein	16								
sll1473		a part of phytochrome-like sensor histidine kinase gene (disrupted by insertion of IS)	16	0,010		1,15					
slr1736		homogentisate phytyltransferase	16								
sll1314		putative C4-dicarboxylase binding protein, periplasmic protein	16								
slr1046		putative TatA protein	16								
sll1507		salt-induced periplasmic protein	16								
16,3	Hypothetical / periplasmic protein identified in proteome		16								
slr2005		periplasmic protein, function unknown	16								
sll1835		periplasmic protein, function unknown	16								
slr1160		periplasmic protein, function unknown	16	0.037 / 0.034	-0,44					-1,02	
sll1483		periplasmic protein, similar to transforming growth factor induced protein	16								
sll1667		periplasmic protein, similar to mitochondrial outer membrane 72K protein	16								
slr1513		periplasmic protein, function unknown	16								
sll1307		periplasmic protein, function unknown	16								
slr1270		periplasmic protein, function unknown	16	0,035						-0,45	
slr1940		periplasmic protein, function unknown	16	0,030					-1,24		
sll0638		periplasmic protein, function unknown	16								
sll0319		periplasmic protein, function unknown	16								
sll1380		periplasmic protein, function unknown	16								
slr2144		periplasmic protein, function unknown	16	0,031					-0,72		
sll0837		periplasmic protein, function unknown	16								
slr0924		periplasmic protein, function unknown	16								
sll0314		periplasmic protein, function unknown	16								
slr1196		periplasmic protein, function unknown	16								
sll1378		periplasmic protein, function unknown	16								
slr1406		periplasmic protein, function unknown	16								
slr1944		periplasmic protein, function unknown	16								
16,4	Hypothetical protein		16								
slr0695		hypothetical protein	16								
slr0680		hypothetical protein	16								
slr1177		hypothetical protein	16								
sll0253		hypothetical protein	16	0,043						1,55	
slr0144		hypothetical protein	16	0,035						1,09	
sll1638		hypothetical protein	16	0,022					0,86		
slr1634		hypothetical protein	16	0.011 / 0.004					0,78		0,96
sll0577		hypothetical protein	16								
slr0244		hypothetical protein	16	0,024		0,21					
sll0735		hypothetical protein	16	0.018 / 0.021					0,55	-0,92	
sgl0002		hypothetical protein	16								
ssr2062		hypothetical protein	16	0,009							-1,91
slr2070		hypothetical protein	16								
slr0013		hypothetical protein	16								
ssr1528		hypothetical protein	16								

sll0529		hypothetical protein	16	0,030							0,58
slr1470		hypothetical protein	16								
ssr3304		hypothetical protein	16								
sll0615		hypothetical protein	16								
sll0487		hypothetical protein	16								
slr1394		hypothetical protein	16	0,019					0,3		
slr0888		hypothetical protein	16								
slr0438		hypothetical protein	16								
sll1390		hypothetical protein	16								
slr1600		hypothetical protein	16								
slr2025		hypothetical protein	16								
slr1649		hypothetical protein	16								
slr0110		hypothetical protein	16								
ssl1498		hypothetical protein	16								
sll1414		hypothetical protein	16	0.041 / 0.036	-0,63					-0,78	
sll1979		hypothetical protein	16								
slr0607		hypothetical protein	16	0,025			0,39				
sll1925		hypothetical protein	16								
slr0887		hypothetical protein	16								
sll1022		hypothetical protein	16								
slr1935		hypothetical protein	16	0,037					0,38		
sll1654		hypothetical protein	16								
slr0172		hypothetical protein	16								
sll1532		hypothetical protein	16								
slr1097		hypothetical protein	16								
slr0516		hypothetical protein	16								
sll1092		hypothetical protein	16	0,017							-0,96
sll0736		hypothetical protein	16	0,042					-0,77		
slr0589		hypothetical protein	16								
sll1783		hypothetical protein	16								
ssl0483		hypothetical protein	16								
slr1692		hypothetical protein	16	0,013							-0,28
ssr1251		hypothetical protein	16								
slr2052		hypothetical protein	16	0,046							0,72
sll0543		hypothetical protein	16								
slr1702		hypothetical protein	16								
ssl3291		hypothetical protein	16								
ssl0105		hypothetical protein	16								
slr1599		hypothetical protein	16								
slr0575		hypothetical protein	16	0,021						-0,24	
slr0217		hypothetical protein	16	0,043							-0,5
ssl1046		hypothetical protein	16								
sll0685		hypothetical protein	16								
slr0147		hypothetical protein	16								
slr0148		hypothetical protein	16	0,011						1,25	
slr0149		hypothetical protein	16								
ssl3177		hypothetical protein	16	0,043						-0,25	
ssl2148		hypothetical protein	16	0.045 / 0.045					1,29		-0,5
slr1800		hypothetical protein	16								
sll0372		hypothetical protein	16								
sll0098		hypothetical protein	16								
slr0552		hypothetical protein	16								
slr1275		hypothetical protein	16								
slr0959		hypothetical protein	16								
slr1535		hypothetical protein	16								
slr0773		hypothetical protein	16	0,029					-0,43		
ssr1951		hypothetical protein	16								
slr1546		hypothetical protein	16								
slr0551		hypothetical protein	16								
slr1173		hypothetical protein	16								
slr0250		hypothetical protein	16								
slr0565		hypothetical protein	16								
sll1866		hypothetical protein	16								
ssr2611		hypothetical protein	16								
ssr1698		hypothetical protein	16								
slr0287		hypothetical protein	16								
ssr1375		hypothetical protein	16								
slr1438		hypothetical protein	16								
slr0954		hypothetical protein	16								
slr1425		hypothetical protein	16								
slr1472		hypothetical protein	16								
slr0241		hypothetical protein	16								
slr0146		hypothetical protein	16								
slr0588		hypothetical protein	16								
sll2002		hypothetical protein	16	0,036			-0,4				
ssl3829		hypothetical protein	16								
sll0932		hypothetical protein	16								
slr0742		hypothetical protein	16	0,011					0,84		
slr1098		hypothetical protein	16								
slr0990		hypothetical protein	16								

slr1623		hypothetical protein	16	0,036				0,88		
slr0243		hypothetical protein	16								
slr0400		hypothetical protein	16								
slr1431		hypothetical protein	16								
slr0443		hypothetical protein	16	0,030					-0,57		
ssl3379		hypothetical protein	16								
ssr1238		hypothetical protein	16								
slr1964		hypothetical protein	16								
ssr2803		hypothetical protein	16								
sll1825		hypothetical protein	16								
slr2084		hypothetical protein	16								
slr0263		hypothetical protein	16								
ssr2009		hypothetical protein	16								
slr1770		hypothetical protein	16	0.005 / 0.007		1,07			1,46		
sll1251		hypothetical protein	16								
slr1612		hypothetical protein	16								
slr0957		hypothetical protein	16								
sll0261		hypothetical protein	16								
slr0374		hypothetical protein	16								
slr1378		hypothetical protein	16								
slr1119		hypothetical protein	16								
slr1611		hypothetical protein	16	0,028							-0,65
sll0787		hypothetical protein	16								
slr0975		hypothetical protein	16	0,004							-0,39
slr1657		hypothetical protein	16	0,036							-0,76
slr0292		hypothetical protein	16								
slr1593		hypothetical protein	16								
slr0740		hypothetical protein	16	0,028							-0,21
slr0976		hypothetical protein	16	0,037							-1,01
sll1039		hypothetical protein	16								
slr0981		hypothetical protein	16								
slr0376		hypothetical protein	16	0,028							-0,85
sll1634		hypothetical protein	16								
ssl1918		hypothetical protein	16								
sll0995		hypothetical protein	16	0,044			0,4				
sll0208		hypothetical protein	16								
sll1355		hypothetical protein	16								
slr1676		hypothetical protein	16	0,035					0,52		
slr1659		hypothetical protein	16								
slr1999		hypothetical protein	16	0,030				0,87			
sll1692		hypothetical protein	16								
slr0326		hypothetical protein	16								
ssl2648		hypothetical protein	16								
sll0565		hypothetical protein	16	0,007				0,32			
sll0325		hypothetical protein	16								
sll1477		hypothetical protein	16								
ssl1807		hypothetical protein	16	0,004				0,91			
slr0978		hypothetical protein	16								
ssl1004		hypothetical protein	16								
sll1573		hypothetical protein	16	0,047					0,96		
sll0925		hypothetical protein	16								
ssl0832		hypothetical protein	16								
slr0423		hypothetical protein	16								
slr0445		hypothetical protein	16	0,012				1,14			
ssr1966		hypothetical protein	16								
sll1247		hypothetical protein	16								
sll2015		hypothetical protein	16								
slr0751		hypothetical protein	16								
sll0752		hypothetical protein	16								
slr0031		hypothetical protein	16								
ssl0352		hypothetical protein	16								
slr1188		hypothetical protein	16								
sll0183		hypothetical protein	16								
sll0888		hypothetical protein	16	0,007				-1,15			
ssr2723		hypothetical protein	16								
slr1104		hypothetical protein	16								
sll1675		hypothetical protein	16	0,027							-1,7
sll1698		hypothetical protein	16								
slr1826		hypothetical protein	16	0,005							-0,51
slr0337		hypothetical protein	16	0,031				0,66			
sll0268		hypothetical protein	16								
slr0645		hypothetical protein	16								
slr0771		hypothetical protein	16								
sll0740		hypothetical protein	16								
slr0852		hypothetical protein	16								
slr0440		hypothetical protein	16								
slr1411		hypothetical protein	16								
slr0769		hypothetical protein	16								
slr1583		hypothetical protein	16	0,024							0,65
slr0192		hypothetical protein	16								

sll0157		hypothetical protein	16							
slr1178		hypothetical protein	16	0,020						0,68
slr0810		hypothetical protein	16							
sll0488		hypothetical protein	16							
ssr0761		hypothetical protein	16							
sll0743		hypothetical protein	16							
ssr2047		hypothetical protein	16							
sll1504		hypothetical protein	16							
slr0755		hypothetical protein	16	0,003					-1,28	
slr0509		hypothetical protein	16							
sll1505		hypothetical protein	16							
slr0885		hypothetical protein	16							
slr1687		hypothetical protein	16	0,026						0,93
slr1814		hypothetical protein	16							
slr1813		hypothetical protein	16							
slr1811		hypothetical protein	16							
ssr1114		hypothetical protein	16							
slr1614		hypothetical protein	16							
slr1613		hypothetical protein	16							
slr0656		hypothetical protein	16							
sll1542		hypothetical protein	16							
sll0141		hypothetical protein	16	0,047						0,13
sll1769		hypothetical protein	16	0,032					-0,56	
sll1651		hypothetical protein	16							
ssr2754		hypothetical protein	16							
ssr2615		hypothetical protein	16							
slr1338		hypothetical protein	16							
slr1812		hypothetical protein	16							
sll1547		hypothetical protein	16							
sll0205		hypothetical protein	16							
ssl0385		hypothetical protein	16							
slr0605		hypothetical protein	16							
ssr3588		hypothetical protein	16							
sll1166		hypothetical protein	16							
ssr2755		hypothetical protein	16							
slr0304		hypothetical protein	16	0,047				-1,25		
sll0318		hypothetical protein	16							
slr2125		hypothetical protein	16							
sll0827		hypothetical protein	16							
ssr0755		hypothetical protein	16							
ssl2921		hypothetical protein	16							
slr1290		hypothetical protein	16							
ssr2377		hypothetical protein	16							
sll1442		hypothetical protein	16	0,033						0,3
sll1770		hypothetical protein	16							
sll0524		hypothetical protein	16							
slr0876		hypothetical protein	16							
ssl0294		hypothetical protein	16							
sll1715		hypothetical protein	16							
slr0313		hypothetical protein	16							
sll1222		hypothetical protein	16							
slr2128		hypothetical protein	16							
sll1773		hypothetical protein	16							
ssr1765		hypothetical protein	16	0.022 / 0.037				-0,47	-0,47	
ssl3389		hypothetical protein	16							
slr0459		hypothetical protein	16							
sll1671		hypothetical protein	16							
slr0291		hypothetical protein	16	0,035					0,09	
sll1609		hypothetical protein	16							
slr0869		hypothetical protein	16							
sll1054		hypothetical protein	16							
sll1158		hypothetical protein	16							
ssr3189		hypothetical protein	16							
slr0355		hypothetical protein	16	0,014				-1,1		
sll1250		hypothetical protein	16							
slr1462		hypothetical protein	16							
slr0195		hypothetical protein	16							
sll0846		hypothetical protein	16							
slr0554		hypothetical protein	16							
ssr1256		hypothetical protein	16	0,029						-1,11
slr0022		hypothetical protein	16							
slr0199		hypothetical protein	16							
sll1884		hypothetical protein	16							
sll0812		hypothetical protein	16	0.033 / 0.007					-0,3	-0,53
slr1493		hypothetical protein	16							
sll0525		hypothetical protein	16	0,010						
ssr1513		hypothetical protein	16							
slr0479		hypothetical protein	16							
slr0553		hypothetical protein	16							
sll1774		hypothetical protein	16							

sll0800		hypothetical protein	16	0,044						-1,44
slr1712		hypothetical protein	16	0,033						-0,3
sll1201		hypothetical protein	16							
sll0549		hypothetical protein	16							
slr0545		hypothetical protein	16							
sll1274		hypothetical protein	16							
slr1799		hypothetical protein	16							
sll0514		hypothetical protein	16							
sll0983		hypothetical protein	16							
slr0373		hypothetical protein	16							
sll1895		hypothetical protein	16							
slr2003		hypothetical protein	16	0,026					0,38	
sll1659		hypothetical protein	16							
sll0335		hypothetical protein	16							
ssl2999		hypothetical protein	16							
sml0012		hypothetical protein	16							
sll0858		hypothetical protein	16							
ssl2749		hypothetical protein	16							
sll1921		hypothetical protein	16							
slr1440		hypothetical protein	16							
ssr0663		hypothetical protein	16							
slr1661		hypothetical protein	16							
slr1674		hypothetical protein	16	0,020						-0,59
sll0913		hypothetical protein	16							
sll0397		hypothetical protein	16							
slr1287		hypothetical protein	16	0.025 / 0.025		-0,52			-1,33	
sll1123		hypothetical protein	16							
sll1940		hypothetical protein	16	0.016 / 0.001	-0,14				-0,73	
ssl1762		hypothetical protein	16							
slr0264		hypothetical protein	16	0,028					0,23	
sll1969		hypothetical protein	16							
sll1726		hypothetical protein	16							
sll0218		hypothetical protein	16	0,028				-1,86		
sll2011		hypothetical protein	16							
slr2000		hypothetical protein	16							
slr1101		hypothetical protein	16	0,033				-1,08		
sll1961		hypothetical protein	16							
ssr3154		hypothetical protein	16							
slr1301		hypothetical protein	16							
slr1100		hypothetical protein	16							
slr1573		hypothetical protein	16							
sll1541		hypothetical protein	16							
ssr0854		hypothetical protein	16							
slr1220		hypothetical protein	16	0,045	-0,49					
slr0816		hypothetical protein	16							
sll0749		hypothetical protein	16							
ssl3297		hypothetical protein	16							
sll0177		hypothetical protein	16							
sll1658		hypothetical protein	16							
sll1155		hypothetical protein	16							
ssl3549		hypothetical protein	16							
sll1660		hypothetical protein	16							
slr1690		hypothetical protein	16							
slr0592		hypothetical protein	16							
sll1318		hypothetical protein	16							
slr1195		hypothetical protein	16	0,041				-0,46		
slr0971		hypothetical protein	16	0,032					0,42	
slr1752		hypothetical protein	16							
slr0082		hypothetical protein	16							
ssl0090		hypothetical protein	16							
sll0364		hypothetical protein	16							
slr1035		hypothetical protein	16							
slr1415		hypothetical protein	16							
sll1372		hypothetical protein	16							
slr1638		hypothetical protein	16							
sll1632		hypothetical protein	16							
slr1203		hypothetical protein	16							
slr2127		hypothetical protein	16							
sll0063		hypothetical protein	16							
ssr3550		hypothetical protein	16							
slr2092		hypothetical protein	16							
slr0556		hypothetical protein	16							
ssl2781		hypothetical protein	16							
slr1069		hypothetical protein	16							
slr1342		hypothetical protein	16	0,032				-0,68		
sll1752		hypothetical protein	16							
ssr2067		hypothetical protein	16							
slr1209		hypothetical protein	16							
slr1161		hypothetical protein	16							
sll1751		hypothetical protein	16							

slr1590		hypothetical protein	16	0,039					-0,52	
ssl2823		hypothetical protein	16	0,032						0,39
slr1110		hypothetical protein	16							
sll1400		hypothetical protein	16							
slr1847		hypothetical protein	16							
slr0732		hypothetical protein	16							
slr0709		hypothetical protein	16							
sll1643		hypothetical protein	16	0,037					1	
sll1164		hypothetical protein	16	0,034			-0,27			
sll1200		hypothetical protein	16							
sll1874		hypothetical protein	16	0,022				-1,45		
sll1898		hypothetical protein	16							
slr0919		hypothetical protein	16							
slr0404		hypothetical protein	16							
ssl1328		hypothetical protein	16							
slr0686		hypothetical protein	16	0,022			0,29			
slr0870		hypothetical protein	16							
sll0051		hypothetical protein	16							
ssr1473		hypothetical protein	16							
sll0071		hypothetical protein	16							
slr1815		hypothetical protein	16							
ssr1880		hypothetical protein	16							
sll0553		hypothetical protein	16	0,027	0,33					
ssl1255		hypothetical protein	16							
slr0967		hypothetical protein	16							
sll0659		hypothetical protein	16							
ssl1263		hypothetical protein	16							
slr1644		hypothetical protein	16							
sll0585		hypothetical protein	16							
ssr2340		hypothetical protein	16							
slr0889		hypothetical protein	16							
sll0354		hypothetical protein	16							
slr1966		hypothetical protein	16							
sll0862		hypothetical protein	16	0,027	0,36					
ssl1972		hypothetical protein	16							
slr1919		hypothetical protein	16							
slr0305		hypothetical protein	16	0,050					-0,52	
ssl2874		hypothetical protein	16							
sll1106		hypothetical protein	16	0,025					0,51	
ssl0511		hypothetical protein	16							
sll2013		hypothetical protein	16							
slr1471		hypothetical protein	16	0,016						0,38
slr0651		hypothetical protein	16							
slr0921		hypothetical protein	16							
slr0780		hypothetical protein	16							
sll1319		hypothetical protein	16							
sll1500		hypothetical protein	16							
slr1444		hypothetical protein	16							
ssr0332		hypothetical protein	16							
sll0788		hypothetical protein	16							
sll1697		hypothetical protein	16	0,046					-0,33	
sll0814		hypothetical protein	16							
slr1276		hypothetical protein	16							
slr1619		hypothetical protein	16	0,040						-0,58
slr0270		hypothetical protein	16							
slr1259		hypothetical protein	16	0,027					1,85	
slr1260		hypothetical protein	16	0,049						1,16
slr1660		hypothetical protein	16	0,030						-0,33
sll0528		hypothetical protein	16							
slr1704		hypothetical protein	16							
slr1918		hypothetical protein	16							
sll0359		hypothetical protein	16							
sml0011		hypothetical protein	16							
slr2080		hypothetical protein	16	0,049				-0,81		
sll0939		hypothetical protein	16	0,023		0,65				
slr1753		hypothetical protein	16							
slr1819		hypothetical protein	16							
ssr2843		hypothetical protein	16							
slr1261		hypothetical protein	16	0,038					1,95	
sll0997		hypothetical protein	16							
slr1677		hypothetical protein	16							
slr1262		hypothetical protein	16	0,009						1,06
slr2010		hypothetical protein	16	0,021						1,48
smr0015		hypothetical protein	16							
slr1951		hypothetical protein	16							
ssr2554		hypothetical protein	16							
ssr1155		hypothetical protein	16	0,033					1,25	
sll1219		hypothetical protein	16							
sll0803		hypothetical protein	16							
slr1128		hypothetical protein	16							

sml0013		hypothetical protein	16							
slr0815		hypothetical protein	16							
slr0483		hypothetical protein	16							
slr0655		hypothetical protein	16							
ssr0757		hypothetical protein	16							
slr1876		hypothetical protein	16							
slr1820		hypothetical protein	16							
sll0498		hypothetical protein	16							
sll0230		hypothetical protein	16							
slr1376		hypothetical protein	16							
slr1718		hypothetical protein	16	0,013				1,29		
slr1530		hypothetical protein	16							
ssr1041		hypothetical protein	16	0,011						-0,51
sll1072		hypothetical protein	16							
slr0360		hypothetical protein	16							
slr1170		hypothetical protein	16	0,039				-0,46		
sll0283		hypothetical protein	16							
slr0770		hypothetical protein	16							
sll1832		hypothetical protein	16							
sll0036		hypothetical protein	16	0,019						-0,39
sll1512		hypothetical protein	16							
sll1203		hypothetical protein	16							
sll0060		hypothetical protein	16							
ssl3719		hypothetical protein	16							
slr1413		hypothetical protein	16	0,017		0,35				
slr0364		hypothetical protein	16							
slr1913		hypothetical protein	16							
slr2117		hypothetical protein	16							
sll1011		hypothetical protein	16							
sll0602		hypothetical protein	16							
slr0606		hypothetical protein	16							
slr0625		hypothetical protein	16							
sll0162		hypothetical protein	16	0.007 / 0.035	-0,83	-0,78				
sll1150		hypothetical protein	16							
sll1060		hypothetical protein	16							
sll1262		hypothetical protein	16	0,043				0,23		
slr0065		hypothetical protein	16							
sll1119		hypothetical protein	16							
ssr3341		hypothetical protein	16							
sll1696		hypothetical protein	16	0,036	-0,55					
slr1102		hypothetical protein	16							
sll1350		hypothetical protein	16							
slr0801		hypothetical protein	16	0,005				-0,4		
sll1693		hypothetical protein	16							
slr0610		hypothetical protein	16	0,045						-0,61
sll0023		hypothetical protein	16							
sll1543		hypothetical protein	16							
slr0630		hypothetical protein	16							
sll1160		hypothetical protein	16							
ssl2971		hypothetical protein	16							
slr1449		hypothetical protein	16							
ssl2064		hypothetical protein	16							
sll1652		hypothetical protein	16							
slr0941		hypothetical protein	16							
sll1252		hypothetical protein	16	0,048	0,3					
sll1965		hypothetical protein	16							
slr0598		hypothetical protein	16							
ssl1376		hypothetical protein	16							
slr0664		hypothetical protein	16							
slr0845		hypothetical protein	16							
sll0470		hypothetical protein	16							
slr1886		hypothetical protein	16							
slr1039		hypothetical protein	16	0,006				0,17		
sll1526		hypothetical protein	16							
slr1927		hypothetical protein	16	0,041				-0,29		
slr1207		hypothetical protein	16							
ssl2807		hypothetical protein	16							
sll0505		hypothetical protein	16							
slr1572		hypothetical protein	16							
slr1152		hypothetical protein	16							
sll0545		hypothetical protein	16							
slr0001		hypothetical protein	16							
ssl1577		hypothetical protein	16							
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slr1628		hypothetical protein	16							
slr1087		hypothetical protein	16							
slr1911		hypothetical protein	16							
slr1926		hypothetical protein	16	0,005	-0,8					
sll0198		hypothetical protein	16							
sll1913		hypothetical protein	16							

slr0619		hypothetical protein	16							
sll1956		hypothetical protein	16	0,036						-0,45
sll0802		hypothetical protein	16							
slr1215		hypothetical protein	16							
sll0781		hypothetical protein	16	0,016						0,2
slr1816		hypothetical protein	16	0,033						-0,76
sll1581		hypothetical protein	16							
sll0597		hypothetical protein	16							
sll0423		hypothetical protein	16							
slr0076		hypothetical protein	16							
ssr1260		hypothetical protein	16							
sll0727		hypothetical protein	16							
ssl1047		hypothetical protein	16							
sll0180		hypothetical protein	16							
sll0877		hypothetical protein	16							
slr1998		hypothetical protein	16							
sll1025		hypothetical protein	16							
ssl1690		hypothetical protein	16							
slr0846		hypothetical protein	16							
slr0431		hypothetical protein	16							
slr0989		hypothetical protein	16							
slr2121		hypothetical protein	16							
ssr2439		hypothetical protein	16							
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sll1095		hypothetical protein	16							
sll0926		hypothetical protein	16							
slr2013		hypothetical protein	16							
sll0863		hypothetical protein	16	0,046					-0,66	
slr1579		hypothetical protein	16							
sll1642		hypothetical protein	16							
slr1699		hypothetical protein	16							
ssr0349		hypothetical protein	16							
slr1179		hypothetical protein	16							
slr1767		hypothetical protein	16							
ssr1562		hypothetical protein	16							
sll0860		hypothetical protein	16	0,046				-0,49		
sll0933		hypothetical protein	16	0,047					0,38	
slr1566		hypothetical protein	16							
ssr1766		hypothetical protein	16	0,010						-0,4
sll0296		hypothetical protein	16	0,032					1,17	
slr0813		hypothetical protein	16							
ssl1300		hypothetical protein	16	0,031					0,69	
slr2008		hypothetical protein	16	0,018						8,69
slr1506		hypothetical protein	16							
sll0168		hypothetical protein	16							
slr1353		hypothetical protein	16							
sll0189		hypothetical protein	16							
slr0232		hypothetical protein	16							
sgl0001		hypothetical protein	16							
sll0765		hypothetical protein	16							
sll0185		hypothetical protein	16							
sll1021		hypothetical protein	16	0,026				-0,65		
sll0249		hypothetical protein	16							
sll0742		hypothetical protein	16							
slr0848		hypothetical protein	16							
ssl0739		hypothetical protein	16							
slr0284		hypothetical protein	16	0,012				2,11		
sll1024		hypothetical protein	16							
slr2038		hypothetical protein	16							
sll0886		hypothetical protein	16							
sll0451		hypothetical protein	16							
sll1640		hypothetical protein	16							
ssr0515		hypothetical protein	16							
slr1419		hypothetical protein	16							
slr2101		hypothetical protein	16							
smr0013		hypothetical protein	16							
sll1464		hypothetical protein	16	0,032			-0,42			
slr1603		hypothetical protein	16							
slr0362		hypothetical protein	16							
slr1122		hypothetical protein	16							
slr0519		hypothetical protein	16							
slr1273		hypothetical protein	16							
ssl0312		hypothetical protein	16							
sll1880		hypothetical protein	16							
sll1138		hypothetical protein	16							
sll0871		hypothetical protein	16							
slr1547		hypothetical protein	16							
slr0878		hypothetical protein	16							
slr1577		hypothetical protein	16							
slr0812		hypothetical protein	16							

sll1995		hypothetical protein	16	0,038				0,43		
sll0310		hypothetical protein	16								
sll1608		hypothetical protein	16								
sll1109		hypothetical protein	16								
sll0822		hypothetical protein	16								
slr1362		hypothetical protein	16								
sll0732		hypothetical protein	16								
ssr1258		hypothetical protein	16								
sll0691		hypothetical protein	16	0,043					0,46		
sll1749		hypothetical protein	16								
ssl2069		hypothetical protein	16								
ssl2733		hypothetical protein	16								
ssr2130		hypothetical protein	16								
slr1083		hypothetical protein	16								
sll1618		hypothetical protein	16								
sll1121		hypothetical protein	16								
slr0179		hypothetical protein	16								
sll1242		hypothetical protein	16								
sll1897		hypothetical protein	16	0,002				0,57			
ssl3692		hypothetical protein	16								
slr0650		hypothetical protein	16								
sll0072		hypothetical protein	16								
slr0397		hypothetical protein	16								
sll1686		hypothetical protein	16								
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sll1280		hypothetical protein	16								
slr0039		hypothetical protein	16								
sll1757		hypothetical protein	16								
slr1186		hypothetical protein	16								
ssl2595		hypothetical protein	16								
sll1601		hypothetical protein	16								
ssl3712		hypothetical protein	16								
slr0249		hypothetical protein	16	0,035	0,73						
sll0658		hypothetical protein	16								
sll1911		hypothetical protein	16								
sll0639		hypothetical protein	16								
slr1236		hypothetical protein	16								
sll0839		hypothetical protein	16								
sll1973		hypothetical protein	16	0,035							0,33
slr1339		hypothetical protein	16								
slr0181		hypothetical protein	16								
slr0053		hypothetical protein	16								
sll0471		hypothetical protein	16								
slr0104		hypothetical protein	16								
sll0175		hypothetical protein	16								
slr1363		hypothetical protein	16								
slr1957		hypothetical protein	16	0,015							-0,62
ssr3000		hypothetical protein	16								
sll1722		hypothetical protein	16								
sll1188		hypothetical protein	16								
slr0883		hypothetical protein	16								
slr1068		hypothetical protein	16								
sll1628		hypothetical protein	16								
slr0863		hypothetical protein	16	0,021				0,47			
slr0285		hypothetical protein	16								
ssl2471		hypothetical protein	16								
sll1415		hypothetical protein	16								
slr0586		hypothetical protein	16								
slr0208		hypothetical protein	16								
slr1915		hypothetical protein	16	0,014							-0,37
slr1048		hypothetical protein	16								
ssr0692		hypothetical protein	16								
slr1050		hypothetical protein	16								
sll0298		hypothetical protein	16	0,034							0,12
slr1327		hypothetical protein	16								
slr2122		hypothetical protein	16								
sll0864		hypothetical protein	16								
sll0905		hypothetical protein	16	0,020					0,77		
sll1193		hypothetical protein	16								
slr1241		hypothetical protein	16								
sll1447		hypothetical protein	16								
ssl0353		hypothetical protein	16								
ssr2016		hypothetical protein	16								
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slr1206		hypothetical protein	16								
slr1568		hypothetical protein	16								
sll0462		hypothetical protein	16								
ssl3573		hypothetical protein	16								
slr1235		hypothetical protein	16								

slr0779		hypothetical protein	16	0,046					0,9		
ssr3122		hypothetical protein	16								
ssr3188		hypothetical protein	16								
slr1081		hypothetical protein	16								
slr1541		hypothetical protein	16								
slr1052		hypothetical protein	16								
sll0898		hypothetical protein	16	0,032							0,39
slr1288		hypothetical protein	16								
sll1118		hypothetical protein	16								
sll2007		hypothetical protein	16								
slr1025		hypothetical protein	16								
sll0082		hypothetical protein	16								
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slr1194		hypothetical protein	16								
slr0842		hypothetical protein	16								
slr0211		hypothetical protein	16								
slr0348		hypothetical protein	16	0,029					-1,31		
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slr1114		hypothetical protein	16								
sll0149		hypothetical protein	16								
ssr2066		hypothetical protein	16								
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slr1184		hypothetical protein	16								
ssr0109		hypothetical protein	16								
slr0980		hypothetical protein	16								
sll1399		hypothetical protein	16	0,023					0,5		
slr0609		hypothetical protein	16								
slr1971		hypothetical protein	16								
sll0400		hypothetical protein	16	0,038					0,26		
sll0350		hypothetical protein	16	0,017	0,52						
slr0300		hypothetical protein	16	0.037 / 0.001		-0,09				0,44	
ssr2802		hypothetical protein	16								
slr1117		hypothetical protein	16	0,029							-0,45
slr1429		hypothetical protein	16	0,019			0,28				
ssr0336		hypothetical protein	16								
ssl0241		hypothetical protein	16								
ssl3446		hypothetical protein	16								
slr1906		hypothetical protein	16								
sll0424		hypothetical protein	16								
slr0510		hypothetical protein	16								
slr1047		hypothetical protein	16								
slr1570		hypothetical protein	16								
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slr1875		hypothetical protein	16								
sll1053		hypothetical protein	16								
slr1565		hypothetical protein	16								
slr0380		hypothetical protein	16	0,043					-0,83		
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ssr2710		hypothetical protein	16								
ssr0657		hypothetical protein	16								
ssl3342		hypothetical protein	16								
slr0207		hypothetical protein	16								
ssl2920		hypothetical protein	16								
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sll1004		hypothetical protein	16								
slr0238		hypothetical protein	16								
sll0360		hypothetical protein	16								
slr1796		hypothetical protein	16								
slr0317		hypothetical protein	16								
sll0924		hypothetical protein	16								
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ssl3803		hypothetical protein	16								
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sll1938		hypothetical protein	16								
slr2141		hypothetical protein	16								
ssl0331		hypothetical protein	16								
slr0142		hypothetical protein	16	0,043							-0,66
sll1691		hypothetical protein	16								
sll0853		hypothetical protein	16								
slr1306		hypothetical protein	16								
sll1775		hypothetical protein	16								
sll1906		hypothetical protein	16								
slr1870		hypothetical protein	16	0,037						0,38	
slr1896		hypothetical protein	16								
sll0361		hypothetical protein	16								
sll1169		hypothetical protein	16								
slr2120		hypothetical protein	16	0,025						0,06	
ssr1391		hypothetical protein	16								

ssr1499		hypothetical protein	16							
slr0121		hypothetical protein	16	0,048						0,39
slr0730		hypothetical protein	16							
sll0355		hypothetical protein	16							
slr0964		hypothetical protein	16	0,045				-0,19		
slr0049		hypothetical protein	16	0,038				-1,03		
slr2103		hypothetical protein	16							
slr0267		hypothetical protein	16							
slr1303		hypothetical protein	16	0,040					-0,34	
sll0572		hypothetical protein	16							
slr1732		hypothetical protein	16	0,012						-0,86
slr0688		hypothetical protein	16							
ssr2087		hypothetical protein	16							
sll1834		hypothetical protein	16							
sll1233		hypothetical protein	16							
slr0119		hypothetical protein	16							
slr1307		hypothetical protein	16							
sll0154		hypothetical protein	16	0,047						0,25
slr0505		hypothetical protein	16	0,044						-0,25
slr0613		hypothetical protein	16							
slr0723		hypothetical protein	16							
slr0455		hypothetical protein	16							
slr1790		hypothetical protein	16							
slr1851		hypothetical protein	16							
sll0596		hypothetical protein	16							
sll2006		hypothetical protein	16							
ssr1558		hypothetical protein	16							
sll1738		hypothetical protein	16							
sll0069		hypothetical protein	16							
slr1174		hypothetical protein	16	0,018						-0,3
sll0160		hypothetical protein	16	0,032					-0,54	
sll1926		hypothetical protein	16	0,031						-0,25
slr0722		hypothetical protein	16							
sll1340		hypothetical protein	16							
sll0994		hypothetical protein	16							
slr1507		hypothetical protein	16							
slr1266		hypothetical protein	16							
slr2012		hypothetical protein	16							
ssr2551		hypothetical protein	16							
slr0765		hypothetical protein	16							
sll0297		hypothetical protein	16							
slr0058		hypothetical protein	16							
slr1977		hypothetical protein	16							
slr1978		hypothetical protein	16	0,040					0,35	
slr0787		hypothetical protein	16	0,028	0,08					
sll1446		hypothetical protein	16	0,012				-0,31		
sll1142		hypothetical protein	16							
sll0413		hypothetical protein	16							
slr1478		hypothetical protein	16							
sll0564		hypothetical protein	16							
slr1223		hypothetical protein	16							
slr0725		hypothetical protein	16							
ssr0756		hypothetical protein	16							
sll1656		hypothetical protein	16							
slr0731		hypothetical protein	16							
slr1914		hypothetical protein	16							
sll0102		hypothetical protein	16							
sll1162		hypothetical protein	16							
sll0007		hypothetical protein	16	0,029		-0,05				
sll0513		hypothetical protein	16							
slr1949		hypothetical protein	16							
slr0930		hypothetical protein	16							
ssl1792		hypothetical protein	16							
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sll0209		hypothetical protein	16							
slr0637		hypothetical protein	16							
sll1386		hypothetical protein	16							
slr1652		hypothetical protein	16							
sll0456		hypothetical protein	16							
slr1495		hypothetical protein	16							
slr0316		hypothetical protein	16							
slr1895		hypothetical protein	16	0,036				-1,11		
slr1344		hypothetical protein	16							
slr0590		hypothetical protein	16							
slr1664		hypothetical protein	16							
slr0517		hypothetical protein	16							
ssr2711		hypothetical protein	16							
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slr1103		hypothetical protein	16							
ssl2009		hypothetical protein	16							

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sll1348		hypothetical protein	16								
ssr1407		hypothetical protein	16								
slr1721		hypothetical protein	16								
sll0147		hypothetical protein	16	0,024			-0,28				
		hypothetical protein	16								
sll1485		hypothetical protein	16								
sll1254		hypothetical protein	16								
sll0037		hypothetical protein	16	0,027							-0,86
slr0491		hypothetical protein	16	0,042							-0,67
ssr2806		hypothetical protein	16								
ssl1377		hypothetical protein	16								
sll1469		hypothetical protein	16								
slr0356		hypothetical protein	16								
slr0821		hypothetical protein	16	0,019							-0,45
slr0280		hypothetical protein	16								
slr0729		hypothetical protein	16								
ssl0788		hypothetical protein	16								
ssr2962		hypothetical protein	16								
slr1464		hypothetical protein	16								
slr0420		hypothetical protein	16	0,032				1,37			
sll0875		hypothetical protein	16								
slr1182		hypothetical protein	16								
slr0254		hypothetical protein	16								
sll1191		hypothetical protein	16	0,015				2,07			
sll0609		hypothetical protein	16								
sll0503		hypothetical protein	16								
sll1902		hypothetical protein	16								
slr1533		hypothetical protein	16								
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sll1232		hypothetical protein	16								
slr1724		hypothetical protein	16								
sll0103		hypothetical protein	16								
sll1063		hypothetical protein	16								
sll1736		hypothetical protein	16								
slr1263		hypothetical protein	16								
ssl0461		hypothetical protein	16	0,007				1,57			
ssr2998		hypothetical protein	16								
sll1285		hypothetical protein	16								
slr1946		hypothetical protein	16								
ssl0259		hypothetical protein	16								
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slr0865		hypothetical protein	16								
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slr0299		hypothetical protein	16								
sll1766		hypothetical protein	16								
sll1934		hypothetical protein	16								
ssl0242		hypothetical protein	16								
ssr1552		hypothetical protein	16								
slr0594		hypothetical protein	16	0,036					0,28		
slr1534		hypothetical protein	16								
slr1648		hypothetical protein	16								
ssl1045		hypothetical protein	16								
slr0789		hypothetical protein	16								
sll0544		hypothetical protein	16								
slr0712		hypothetical protein	16								
ssl1923		hypothetical protein	16								
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slr2006		hypothetical protein	16								
ssl2717		hypothetical protein	16								
slr2105		hypothetical protein	16								
slr1094		hypothetical protein	16								
sll1886		hypothetical protein	16								
sll0005		hypothetical protein	16	0,034				0,32			
slr0325		hypothetical protein	16	0,010							-0,67
sll0272		hypothetical protein	16								
slr1461		hypothetical protein	16								
sll0854		hypothetical protein	16	0,035					-0,84		
slr0689		hypothetical protein	16								
ssr3571		hypothetical protein	16								
slr1821		hypothetical protein	16	0,017				0,37			
sll0496		hypothetical protein	16	0,046							-0,34
sll0809		hypothetical protein	16								
sll0148		hypothetical protein	16								
ssr2708		hypothetical protein	16								
sll1071		hypothetical protein	16								
slr1900		hypothetical protein	16								
slr0635		hypothetical protein	16								

sll1606		hypothetical protein	16							
sll0192		hypothetical protein	16							
ssr0550		hypothetical protein	16							
sll0804		hypothetical protein	16							
sll1915		hypothetical protein	16	0,046						0,44
sll0260		hypothetical protein	16							
slr0806		hypothetical protein	16							
slr0303		hypothetical protein	16							
slr1762		hypothetical protein	16							
sll0436		hypothetical protein	16							
slr0734		hypothetical protein	16							
ssl1378		hypothetical protein	16	0,009				-1,05		
slr1384		hypothetical protein	16	0,025				-0,33		
sll0676		hypothetical protein	16	0,012						-0,48
sll0284		hypothetical protein	16							
slr0643		hypothetical protein	16							
sll1488		hypothetical protein	16							
slr0038		hypothetical protein	16							
sll1289		hypothetical protein	16							
sll0586		hypothetical protein	16							
sll1845		hypothetical protein	16							
slr0016		hypothetical protein	16	0,014				-0,37		
ssr3572		hypothetical protein	16							
sll1461		hypothetical protein	16							
sll0611		hypothetical protein	16							
slr1990		hypothetical protein	16							
sll0031		hypothetical protein	16							
slr1970		hypothetical protein	16							
sll1524		hypothetical protein	16							
sll2003		hypothetical protein	16							
slr0064		hypothetical protein	16							
sll1571		hypothetical protein	16							
sll1455		hypothetical protein	16							
sll0414		hypothetical protein	16	0,004					-0,34	
slr1885		hypothetical protein	16							
ssl3451		hypothetical protein	16	0,014						-0,42
slr1717		hypothetical protein	16							
slr1116		hypothetical protein	16							
slr0818		hypothetical protein	16							
sll1144		hypothetical protein	16							
slr0596		hypothetical protein	16							
slr0383		hypothetical protein	16							
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sll1052		hypothetical protein	16							
sll0095		hypothetical protein	16							
sll0257		hypothetical protein	16							
sll0499		hypothetical protein	16							
sll0832		hypothetical protein	16							
slr0359		hypothetical protein	16							
sll0410		hypothetical protein	16							
slr1142		hypothetical protein	16							
sll0174		hypothetical protein	16							
slr1441		hypothetical protein	16							
slr1519		hypothetical protein	16							
sll0497		hypothetical protein	16							
sll0381		hypothetical protein	16							
slr2060		hypothetical protein	16							
slr1827		hypothetical protein	16							
sll0274		hypothetical protein	16							
sll1389		hypothetical protein	16							
slr1442		hypothetical protein	16							
slr1343		hypothetical protein	16							
slr1474		hypothetical protein	16							
sll1367		hypothetical protein	16							
slr1864		hypothetical protein	16	0,016						-0,84
sll0670		hypothetical protein	16	0,022					1,31	
smr0014		hypothetical protein	16							
slr1183		hypothetical protein	16	0,011				-0,66		
sll1376		hypothetical protein	16							
sll1424		hypothetical protein	16							
sll1173		hypothetical protein	16							
sll1960		hypothetical protein	16							
sll0696		hypothetical protein	16							
ssl0258		hypothetical protein	16							
slr0407		hypothetical protein	16	0,021		-0,26				
slr0105		hypothetical protein	16	0,029				-1,01		
slr0642		hypothetical protein	16							
sll0861		hypothetical protein	16							
sll0295		hypothetical protein	16	0,007				-0,52		
slr1095		hypothetical protein	16	0,037						-0,58

slr1143		hypothetical protein	16								
slr0169		hypothetical protein	16								
slr1686		hypothetical protein	16								
slr0388		hypothetical protein	16								
sll0216		hypothetical protein	16								
slr1503		hypothetical protein	16								
sll0944		hypothetical protein	16								
slr1315		hypothetical protein	16								
slr1818		hypothetical protein	16								
slr0784		hypothetical protein	16								
slr0670		hypothetical protein	16								
ssl1707		hypothetical protein	16	0,041					0,68		
sll0737		hypothetical protein	16								
slr1451		hypothetical protein	16								
slr1624		hypothetical protein	16								
sll1433		hypothetical protein	16								
slr0711		hypothetical protein	16								
sll0744		hypothetical protein	16								
slr1468		hypothetical protein	16								
sll0096		hypothetical protein	16								
sll0996		hypothetical protein	16								
sll0532		hypothetical protein	16								
slr0402		hypothetical protein	16								
sll0382		hypothetical protein	16								
sll0178		hypothetical protein	16								
slr0092		hypothetical protein	16								
slr1230		hypothetical protein	16								
sll1916		hypothetical protein	16								
slr1679		hypothetical protein	16	0.03/0.014/0.013/0.005		-0,33			-0,98	-0,5	-0,51
slr1880		hypothetical protein	16								
sll0931		hypothetical protein	16								
slr0728		hypothetical protein	16								
slr2011		hypothetical protein	16	0,011							1,24
sll0412		hypothetical protein	16								
sll1486		hypothetical protein	16	0,025					0,16		
ssr3410		hypothetical protein	16	0,012							1,65
slr1737		hypothetical protein	16								
sll1192		hypothetical protein	16								
sll0606		hypothetical protein	16								
slr1563		hypothetical protein	16								
slr0363		hypothetical protein	16								
sll0442		hypothetical protein	16	0,036		-0,61					
sll1186		hypothetical protein	16								
ssr2781		hypothetical protein	16								
sll1946		hypothetical protein	16								
sll0793		hypothetical protein	16								
sll1388		hypothetical protein	16								
slr1428		hypothetical protein	16	0,033						-0,63	
sll0984		hypothetical protein	16								
slr1840		hypothetical protein	16								
slr0351		hypothetical protein	16								
slr0269		hypothetical protein	16	0,017					-0,7		
slr1807		hypothetical protein	16								
ssr3409		hypothetical protein	16	0.005 / 0.028					-1,53		1,84
sll0867		hypothetical protein	16								
slr0935		hypothetical protein	16								
slr1647		hypothetical protein	16								
slr2042		hypothetical protein	16	0,001					0,41		
sll0301		hypothetical protein	16								
sll1036		hypothetical protein	16								
sll1495		hypothetical protein	16	0,034						-0,83	
ssl0900		hypothetical protein	16								
sll1336		hypothetical protein	16								
slr0487		hypothetical protein	16								
slr0453		hypothetical protein	16								
slr1923		hypothetical protein	16								
slr1917		hypothetical protein	16								
slr0698		hypothetical protein	16								
sll1912		hypothetical protein	16								
sll0294		hypothetical protein	16	0,043							-0,65
sll1381		hypothetical protein	16								
slr0872		hypothetical protein	16								
ssl3382		hypothetical protein	16								
17.1	Unknown / with gene code and functional annotation		17								
sll1687	hik17	unknown protein (histidine kinase)	17	0,015							-0,39
slr1829	phaE	putative poly(3-hydroxyalkanoate) synthase component	17								
slr1456	pilA4	type 4 pilin-like protein, or general secretion pathway protein G	17								
slr1930	pilA7	type 4 pilin-like protein	17	0,046						1,6	

sll1515	gifB	glutamine synthetase inactivating factor IF17	17	0.038 / 0.047		0,5			0,61	
slr0793	nrsB	cation efflux system protein involved in nickel and cobalt tolerance	17							
slr2016	pilA10	type 4 pilin-like protein, essential for motility	17	0,021						1,2
slr2017	pilA11	type 4 pilin-like protein, essential for motility	17	0,049				-0,51		
slr1928	pilA5	type 4 pilin-like protein	17							
slr1931	pilA8	type 4 pilin-like protein	17							
slr2015	pilA9	type 4 pilin-like protein, essential for motility	17							
slr0593	samp	cAMP binding membrane protein	17	0,022						
17,2	Unknown / with functional annotation		17							
slr1485		putative phosphatidylinositol phosphate kinase, salt-induced periplasmic protein	17							
slr0286		protein involved in functional assembly of photosystem II	17							
slr0114		putative PP2C-type protein phosphatase	17							
slr1668		periplasmic protein, function unknown (target gene of sycrp1)	17							
slr1667		hypothetical protein (target gene of sycrp1)	17							
17,3	Unknown / periplasmic protein identified in proteome		17							
sll1306		periplasmic protein, function unknown	17							
sll1784		periplasmic protein, function unknown	17							
sll1785		periplasmic protein, function unknown	17							
slr0708		periplasmic protein, function unknown	17							
sll1089		periplasmic protein, function unknown	17	0,038						1,25
sll1837		periplasmic protein, function unknown	17							
slr2004		periplasmic protein, function unknown	17							
slr0841		periplasmic protein, function unknown	17							
slr2048		periplasmic protein, function unknown	17							
sll0172		periplasmic protein, function unknown	17							
17,4	Unknown / Unknown protein		17							
sll0478		unknown protein	17	0,007						0,2
sll0518		unknown protein	17							
sll1304		unknown protein	17							
sll1456		unknown protein	17							
sll1472		unknown protein	17	0,033			1,8			
sll1583		unknown protein	17							
sll1830		unknown protein	17							
sll1873		unknown protein	17							
slr0145		unknown protein	17							
slr0476		unknown protein	17							
slr1127		unknown protein	17	0.001 / 0.024				1,01		0,34
slr1436		unknown protein	17							
slr1437		unknown protein	17							
slr1852		unknown protein	17	0,025						-0,42
slr1854		unknown protein	17	0,049						-0,56
ssl2138		unknown protein	17							
ssl3383		unknown protein	17							
ssl3410		unknown protein	17							
ssr1038		unknown protein	17	0,005						1,23
ssr2333		unknown protein	17							
sll0595		unknown protein	17	0,037						0,28
sll0656		unknown protein	17							
sll1009		unknown protein	17							
sll1891		unknown protein	17							
slr1855		unknown protein	17							
ssl0787		unknown protein	17							
sll0022		unknown protein	17	0,050	0,43					
sll0263		unknown protein	17	0.045 / 0.016 / 0.013	-0,53	-0,46			-1,46	
sll0376		unknown protein	17	0,004						
sll1130		unknown protein	17	0,008				1,32		
slr0587		unknown protein	17							
ssl2100		unknown protein	17							
ssl2245		unknown protein	17	0,025						-1,25
sll0375		unknown protein	17							
sll0405		unknown protein	17							
sll0762		unknown protein	17							
sll0779		unknown protein	17	0,032	-0,41					-0,3
sll0783		unknown protein	17							
sll0785		unknown protein	17							
sll0810		unknown protein	17							
sll0843		unknown protein	17							
sll0857		unknown protein	17	0,045					1,08	
sll0982		unknown protein	17							
sll1037		unknown protein	17							
sll1236		unknown protein	17							
sll1268		unknown protein	17	0,042					0,71	
sll1338		unknown protein	17							
sll1630		unknown protein	17							
sll1764		unknown protein	17							
sll1885		unknown protein	17	0,049						0,66

sll1939		unknown protein	17							
sll1949		unknown protein	17							
slr0272		unknown protein	17	0,012						0,63
slr0368		unknown protein	17							
slr0489		unknown protein	17							
slr0937		unknown protein	17	0,007				0,52		
slr0960		unknown protein	17	0,006					0,27	
slr1082		unknown protein	17							
slr1189		unknown protein	17							
slr1397		unknown protein	17	0,000						-0,57
slr1450		unknown protein	17							
slr1768		unknown protein	17							
slr1809		unknown protein	17							
ssl0410		unknown protein	17							
ssl1533		unknown protein	17							
ssl2162		unknown protein	17							
ssl2501		unknown protein	17	0,004		0,42				
ssl2507		unknown protein	17							
ssl3615		unknown protein	17							
ssr2318		unknown protein	17							
ssr3467		unknown protein	17							
sll0024		unknown protein	17							
sll0191		unknown protein	17	0,046			0,19			
sll0327		unknown protein	17							
sll0328		unknown protein	17							
sll0371		unknown protein	17							
sll0441		unknown protein	17							
sll0447		unknown protein	17							
sll0448		unknown protein	17							
sll0664		unknown protein	17							
sll0688		unknown protein	17							
sll0909		unknown protein	17	0,030						-0,14
sll1170		unknown protein	17							
sll1225		unknown protein	17							
sll1272		unknown protein	17							
sll1273		unknown protein	17							
sll1396		unknown protein	17							
sll1503		unknown protein	17							
sll1582		unknown protein	17							
sll1611		unknown protein	17							
sll1665		unknown protein	17	0,029			-0,27			
sll1714		unknown protein	17							
sll1717		unknown protein	17							
sll1739		unknown protein	17							
slr0060		unknown protein	17	0,011				-0,7		
slr0294		unknown protein	17							
slr0393		unknown protein	17							
slr0666		unknown protein	17							
slr0867		unknown protein	17							
slr0912		unknown protein	17	0,016					-0,83	
slr1070		unknown protein	17							
slr1074		unknown protein	17	0,037						-1,52
slr1421		unknown protein	17							
slr1616		unknown protein	17	0,000						-0,87
slr1789		unknown protein	17							
slr1980		unknown protein	17							
slr2037		unknown protein	17							
ssl0323		unknown protein	17							
ssl1464		unknown protein	17	0,039					0,61	
ssl2420		unknown protein	17							
ssr0511		unknown protein	17							
ssr0536		unknown protein	17	0,037				-0,46		
sll0010		unknown protein	17							
sll0066		unknown protein	17							
sll0085		unknown protein	17							
sll0156		unknown protein	17							
sll0188		unknown protein	17	0,044		0,52				
sll0252		unknown protein	17							
sll0266		unknown protein	17							
sll0282		unknown protein	17							
sll0406		unknown protein	17							
sll0426		unknown protein	17	0,042						-0,43
sll0508		unknown protein	17							
sll0623		unknown protein	17							
sll0625		unknown protein	17	0,025		0,05				
sll0811		unknown protein	17	0,016				0,55		
sll0943		unknown protein	17							
sll0980		unknown protein	17							
sll1167		unknown protein	17							
sll1862		unknown protein	17							

sll1951		unknown protein	17	0,039						-1,43
slr0103		unknown protein	17							
slr0196		unknown protein	17	0,002						
slr0569		unknown protein	17	0,036				-0,54		
slr0616		unknown protein	17	0,025						0,02
slr0658		unknown protein	17							
slr0868		unknown protein	17	0,020			0,31			
slr1079		unknown protein	17	0,046				-0,53		
slr1168		unknown protein	17							
slr1187		unknown protein	17							
slr1222		unknown protein	17							
slr1788		unknown protein	17	0,002			-0,54			
slr2046		unknown protein	17							
ssl2502		unknown protein	17							
ssl3222		unknown protein	17							
ssr0706		unknown protein	17							
ssr0759		unknown protein	17							
ssr1768		unknown protein	17	0,012						-0,68
ssr2787		unknown protein	17							
ssr2912		unknown protein	17							
sll0101		unknown protein	17							
sll0403		unknown protein	17							
sll0710		unknown protein	17							
sll0775		unknown protein	17							
sll1061		unknown protein	17							
sll1132		unknown protein	17							
sll1239		unknown protein	17							
sll1240		unknown protein	17	0,035		-1,51				
sll1241		unknown protein	17	0.011 / 0.003		-0,69			-1,01	
sll1267		unknown protein	17							
sll1429		unknown protein	17							
sll1531		unknown protein	17							
sll1562		unknown protein	17							
sll1563		unknown protein	17							
sll1613		unknown protein	17							
slr0157		unknown protein	17							
slr0333		unknown protein	17	0,019						-1,59
slr0334		unknown protein	17	0,047						-1,7
slr0522		unknown protein	17							
slr0719		unknown protein	17	0.004 / 0.004					-0,46	0,28
slr0727		unknown protein	17							
slr0871		unknown protein	17							
slr0913		unknown protein	17	0,048						-0,66
slr0914		unknown protein	17							
slr1056		unknown protein	17							
slr1062		unknown protein	17							
slr1071		unknown protein	17							
slr1073		unknown protein	17							
slr1162		unknown protein	17							
slr1243		unknown protein	17							
slr1396		unknown protein	17							
slr1959		unknown protein	17							
slr2110		unknown protein	17							
slr2111		unknown protein	17	0,041		0,51				
slr2115		unknown protein	17							
slr2118		unknown protein	17							
ssl0738		unknown protein	17							
ssl1326		unknown protein	17							
ssr3402		unknown protein	17	0,032						0,99
sll0140		unknown protein	17							
sll0445		unknown protein	17							
sll0446		unknown protein	17	0,006			-0,76			
sll0780		unknown protein	17	0,030						-0,71
sll0911		unknown protein	17							
sll0923		unknown protein	17							
sll1086		unknown protein	17							
sll1293		unknown protein	17							
sll1552		unknown protein	17							
sll1681		unknown protein	17	0,044			0,43			
sll1863		unknown protein	17							
sll1882		unknown protein	17	0,044				1,07		
slr0006		unknown protein	17	0,032						1,19
slr0106		unknown protein	17							
slr0273		unknown protein	17	0,042				0,53		
slr0306		unknown protein	17							
slr0581		unknown protein	17	0.024 / 0.029					0,89	0,57
slr0654		unknown protein	17							
slr0667		unknown protein	17							
slr0962		unknown protein	17							
slr1066		unknown protein	17							

slr1340		unknown protein	17							
slr1403		unknown protein	17	0,040					0,6	
slr1804		unknown protein	17							
ssl2891		unknown protein	17							
ssl2996		unknown protein	17							
ssr0693		unknown protein	17							
ssr1853		unknown protein	17							
ssr2153		unknown protein	17							
ssr2194		unknown protein	17							
ssr3159		unknown protein	17							
ssr3465		unknown protein	17							
sll0008		unknown protein	17							
sll0044		unknown protein	17							
sll0048		unknown protein	17							
sll0068		unknown protein	17							
sll0167		unknown protein	17							
sll0181		unknown protein	17							
sll0225		unknown protein	17							
sll0236		unknown protein	17							
sll0237		unknown protein	17							
sll0238		unknown protein	17							
sll0241		unknown protein	17							
sll0242		unknown protein	17	0.02 / 0.048	-0,59					-0,57
sll0243		unknown protein	17							
sll0265		unknown protein	17							
sll0267		unknown protein	17	0,048			-0,32			
sll0280		unknown protein	17							
sll0281		unknown protein	17							
sll0293		unknown protein	17							
sll0309		unknown protein	17							
sll0321		unknown protein	17							
sll0369		unknown protein	17							
sll0384		unknown protein	17	0,029						-1,37
sll0394		unknown protein	17							
sll0419		unknown protein	17							
sll0428		unknown protein	17							
sll0443		unknown protein	17							
sll0444		unknown protein	17							
sll0449		unknown protein	17	0.028 / 0.025 / 0.016	-0,41	-0,6			-0,78	
sll0473		unknown protein	17							
sll0479		unknown protein	17							
sll0481		unknown protein	17							
sll0482		unknown protein	17							
sll0494		unknown protein	17							
sll0539		unknown protein	17							
sll0547		unknown protein	17							
sll0552		unknown protein	17							
sll0563		unknown protein	17							
sll0588		unknown protein	17	0,032				2,54		
sll0590		unknown protein	17							
sll0614		unknown protein	17							
sll0624		unknown protein	17							
sll0630		unknown protein	17							
sll0641		unknown protein	17							
sll0645		unknown protein	17							
sll0647		unknown protein	17							
sll0669		unknown protein	17							
sll0702		unknown protein	17							
sll0703		unknown protein	17							
sll0721		unknown protein	17							
sll0722		unknown protein	17							
sll0723		unknown protein	17							
sll0733		unknown protein	17							
sll0756		unknown protein	17							
sll0761		unknown protein	17							
sll0786		unknown protein	17							
sll0815		unknown protein	17							
sll0847		unknown protein	17							
sll0872		unknown protein	17							
sll0910		unknown protein	17							
sll0914		unknown protein	17							
sll0922		unknown protein	17							
sll0930		unknown protein	17	0,005						-0,45
sll0981		unknown protein	17							
sll0985		unknown protein	17							
sll1006		unknown protein	17							
sll1040		unknown protein	17	0,039						0,15
sll1062		unknown protein	17							
sll1068		unknown protein	17							
sll1131		unknown protein	17							

sll1135		unknown protein	17	0,002					0,49	
sll1151		unknown protein	17							
sll1163		unknown protein	17	0,043						-0,34
sll1174		unknown protein	17	0,031						-0,43
sll1217		unknown protein	17							
sll1265		unknown protein	17	0.004 / 0.005				-0,53	0,71	
sll1315		unknown protein	17							
sll1333		unknown protein	17							
sll1344		unknown protein	17							
sll1352		unknown protein	17							
sll1359		unknown protein	17							
sll1365		unknown protein	17							
sll1373		unknown protein	17							
sll1401		unknown protein	17							
sll1426		unknown protein	17							
sll1439		unknown protein	17							
sll1476		unknown protein	17	0,025				0,98		
sll1510		unknown protein	17	0,006			-0,51			
sll1511		unknown protein	17	0,036				0,25		
sll1527		unknown protein	17							
sll1528		unknown protein	17	0.04 / 0.041				-0,6		0,61
sll1530		unknown protein	17							
sll1570		unknown protein	17							
sll1586		unknown protein	17							
sll1730		unknown protein	17							
sll1755		unknown protein	17							
sll1761		unknown protein	17							
sll1763		unknown protein	17	0,020					-0,99	
sll1765		unknown protein	17							
sll1851		unknown protein	17							
sll1853		unknown protein	17	0,002						0,63
sll1858		unknown protein	17							
sll1892		unknown protein	17							
sll1942		unknown protein	17							
sll1950		unknown protein	17							
sll1954		unknown protein	17							
slr0019		unknown protein	17	0,018				1,28		
slr0023		unknown protein	17							
slr0059		unknown protein	17							
slr0061		unknown protein	17							
slr0069		unknown protein	17	0,047					-0,74	
slr0108		unknown protein	17							
slr0109		unknown protein	17							
slr0111		unknown protein	17							
slr0112		unknown protein	17							
slr0151		unknown protein	17	0,031					0,78	
slr0168		unknown protein	17	0,037					-0,62	
slr0184		unknown protein	17							
slr0209		unknown protein	17							
slr0226			17							
slr0262		unknown protein	17							
slr0271		unknown protein	17	0,039			1,03			
slr0302		unknown protein	17							
slr0318		unknown protein	17	0,004						0,24
slr0341		unknown protein	17							
slr0345		unknown protein	17							
slr0353		unknown protein	17	0.039 / 0.002	0,3	0,7				
slr0358		unknown protein	17							
slr0366		unknown protein	17	0,005				-0,28		
slr0377		unknown protein	17							
slr0386		unknown protein	17							
slr0392		unknown protein	17							
slr0398		unknown protein	17							
slr0408		unknown protein	17							
slr0416		unknown protein	17							
slr0421		unknown protein	17							
slr0439		unknown protein	17							
slr0442		unknown protein	17							
slr0456		unknown protein	17							
slr0458		unknown protein	17							
slr0468		unknown protein	17							
slr0482		unknown protein	17							
slr0496		unknown protein	17	0,010						-0,48
slr0498		unknown protein	17							
slr0514		unknown protein	17							
slr0521		unknown protein	17	0,020					-0,58	
slr0572		unknown protein	17	0,030		1,35				
slr0573		unknown protein	17							
slr0579		unknown protein	17	0,002					1,02	
slr0582		unknown protein	17	0,027					0,8	

slr0601		unknown protein	17							
slr0602		unknown protein	17							
slr0617		unknown protein	17	0,016	0,6					
slr0634		unknown protein	17							
slr0668		unknown protein	17							
slr0675		unknown protein	17							
slr0699		unknown protein	17	0.0281 / 1.22e-02		-0,41			-1,3	
slr0702		unknown protein	17							
slr0829		unknown protein	17							
slr0881		unknown protein	17	0,045					0,8	
slr0890		unknown protein	17	0.024 / 0.031					1,05	-0,32
slr0907		unknown protein	17							
slr0909		unknown protein	17							
slr1023		unknown protein	17							
slr1028		unknown protein	17							
slr1032		unknown protein	17	0,027						-0,59
slr1033		unknown protein	17	0,029						-0,67
slr1053		unknown protein	17	0,018					-1,13	
slr1084		unknown protein	17							
slr1107		unknown protein	17	0,035				-0,87		
slr1135		unknown protein	17							
slr1148		unknown protein	17							
slr1150		unknown protein	17							
slr1163		unknown protein	17							
slr1169		unknown protein	17							
slr1210		unknown protein	17							
slr1232		unknown protein	17	0,009					0,89	
slr1240		unknown protein	17							
slr1253		unknown protein	17							
slr1257		unknown protein	17	0,047					-0,3	
slr1258		unknown protein	17							
slr1298		unknown protein	17							
slr1383		unknown protein	17							
slr1385		unknown protein	17							
slr1391		unknown protein	17							
slr1398		unknown protein	17							
slr1407		unknown protein	17							
slr1475		unknown protein	17							
slr1484		unknown protein	17							
slr1505		unknown protein	17							
slr1537		unknown protein	17							
slr1544		unknown protein	17	0,012						0,94
slr1552		unknown protein	17							
slr1567		unknown protein	17							
slr1571		unknown protein	17							
slr1576		unknown protein	17							
slr1618		unknown protein	17							
slr1627		unknown protein	17							
slr1636		unknown protein	17							
slr1658		unknown protein	17							
slr1670		unknown protein	17							
slr1681		unknown protein	17							
slr1726		unknown protein	17							
slr1771		unknown protein	17							
slr1773		unknown protein	17							
slr1774		unknown protein	17							
slr1778		unknown protein	17							
slr1798		unknown protein	17							
slr1862		unknown protein	17							
slr1863		unknown protein	17							
slr1865		unknown protein	17	0,036			-0,35			
slr1866		unknown protein	17	0,043						-0,69
slr1869		unknown protein	17							
slr1920		unknown protein	17	0.01 / 0.03	-0,49				-1,41	
slr1932		unknown protein	17							
slr1939		unknown protein	17							
slr1956		unknown protein	17							
slr1958		unknown protein	17							
slr1968		unknown protein	17							
slr2018		unknown protein	17	0,014						0,94
slr2027		unknown protein	17							
slr2071		unknown protein	17	0,037					0,87	
slr2119		unknown protein	17	0,037					0,32	
ssl0109		unknown protein	17							
ssl0318		unknown protein	17							
ssl0350		unknown protein	17							
ssl0431		unknown protein	17							
ssl0467		unknown protein	17							
ssl0606		unknown protein	17							
ssl0750		unknown protein	17							

ssl1493		unknown protein	17							
ssl1520		unknown protein	17							
ssl1552		unknown protein	17							
ssl2065		unknown protein	17							
ssl2380		unknown protein	17							
ssl2384		unknown protein	17							
ssl2653		unknown protein	17							
ssl2814		unknown protein	17							
ssl3076		unknown protein	17							
ssl3142		unknown protein	17							
ssl3769		unknown protein	17							
ssr0335		unknown protein	17							
ssr0680		unknown protein	17							
ssr1049		unknown protein	17							
ssr1274		unknown protein	17							
ssr2049		unknown protein	17							
ssr2060		unknown protein	17	0,034			0,59			
ssr2201		unknown protein	17	0,030				-0,53		
ssr2254		unknown protein	17							
ssr2317		unknown protein	17							
ssr2406		unknown protein	17							
ssr2422		unknown protein	17	0,014					0,74	
ssr2549		unknown protein	17							
ssr2553		unknown protein	17							
ssr2848		unknown protein	17	0.012 / 0.038					1,18	1,18
ssr2972		unknown protein	17							
ssr2975		unknown protein	17							
ssr3129		unknown protein	17							
ssr3300		unknown protein	17							
ssr3532		unknown protein	17							
ssr3570		unknown protein	17	0,017				0,91		

EIDESSTATTLICHE ERKLÄRUNG

Hiermit versichere ich, die vorliegende Dissertation eigenständig verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel verwendet zu haben. Die dem Verfahren zugrunde liegende Promotionsordnung ist mir bekannt.

Die Dissertation wurde in der jetzigen oder einer ähnlichen Form bei keiner anderen Hochschule eingereicht und hat noch keinen sonstigen Prüfungszwecken gedient.

Acknowledgements

First and foremost I would like to thank my supervisor Thomas Börner, he has been for great help in every possible way and an inspiration throughout the time.

I am also very grateful to the whole team of the company Cyano Biofuels GmbH and its CEO Dan Kramer. It was a real pleasure to cooperate and the meetings have been a real place for open thinking and innovation. I learned a lot and had a wonderful time for which I wanted to thank every participant. To all my co-worker, I hope you all know how much I appreciated the time with you all. Last but not least I wanted of course give my thanks to my family, my wife, my mother and my baby girl Luna. These are all your achievements!